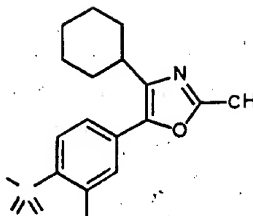


-318-

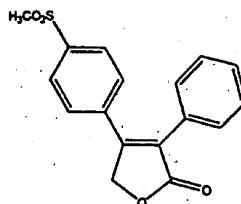
1)



Sub 1  
a  
Cont

-319-

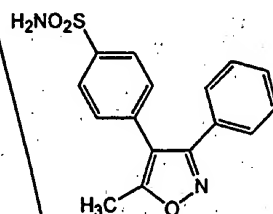
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone,

5

6)



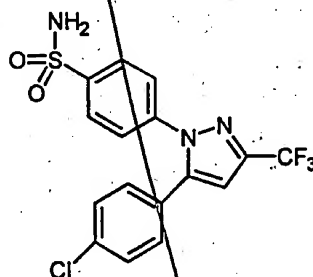
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

7)

N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide,

10

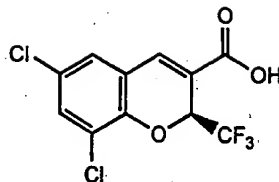
8)



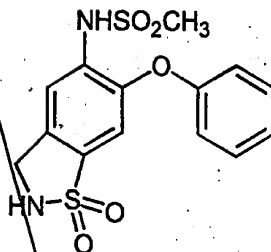
4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,

-320-

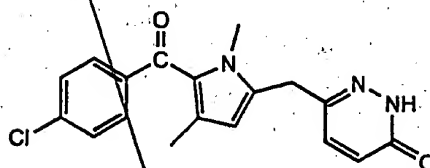
9)



10)

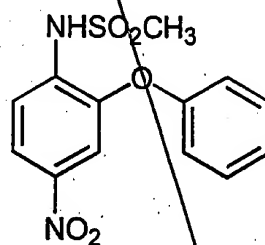


11)



6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

12)



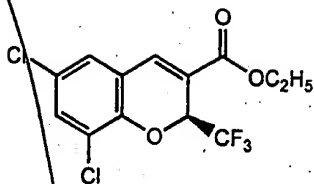
N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

10

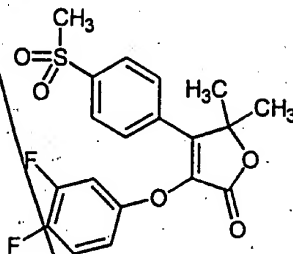
Sub  
a  
Cent  
0860063.100501  
T05001.290000

-321-

13)



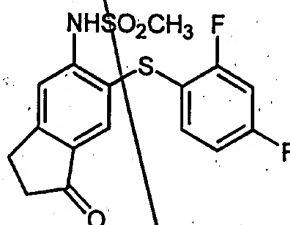
14)



5

3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

15)

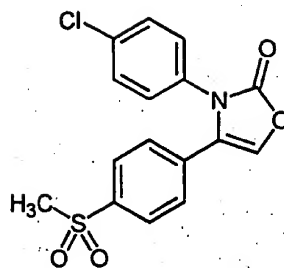


N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

10

Subal  
105001-105003

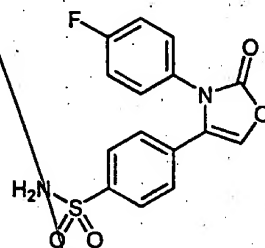
16)



3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

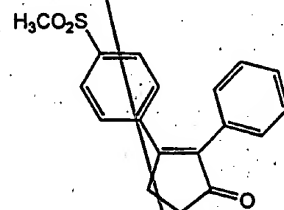
5

17)



4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



10

3-[4-(methylsulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

098600501

Sub 1  
Cont

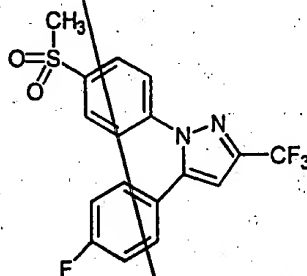
-323-

Cc1nc2c(c1)ccc2-c3ccc(cc3)S(=O)(=O)N

5 20)

Cs1cc(ccc1S(=O)(=O)c2ccc(cc2)c3c[nH]c4cc(F)ccc43)c5ccccc5

21)



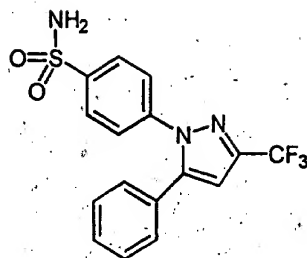
10

**SECRET**

Just a  
bunt

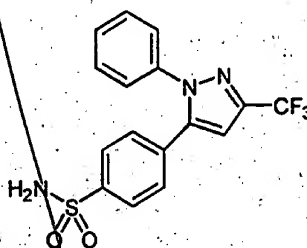
-324-

22)



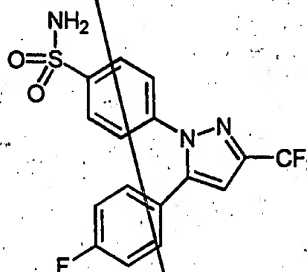
4-[5-phenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

5 23)



4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl]benzenesulfonamide,

24)



4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

10

-325-

COS(=O)c1ccc(cc1)OC2CCCCC2

26)

COS(=O)(=O)c1ccc(Oc2ccc(F)c(F)c2)c3ccccc3C4=CC(=O)CC4

27)

CC(=O)NS(=O)(=O)c1ccc(OC2=CC=C(C=C2)Cl)cc1

3-(4-chlorophenoxy)-4-  
[(methylsulfonyl)amino]benzenesulfonamide,

10

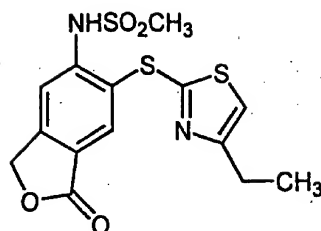
Suba Cont





-327-

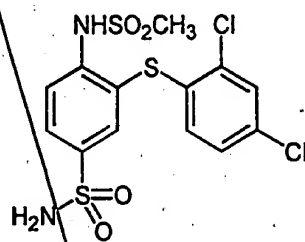
31)



N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

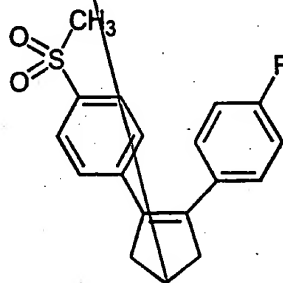
5

32)



3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino]benzenesulfonamide,

33)



10

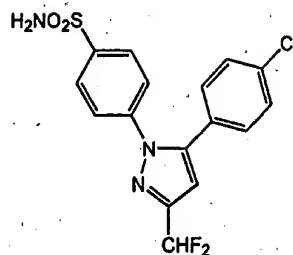
1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,

TO500T-0099950

Sub 1  
Cont

-328-

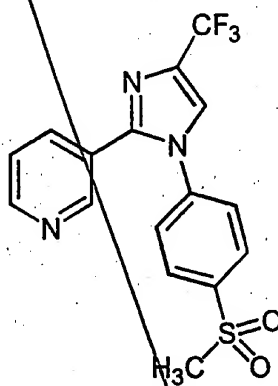
34)



4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

5

35)



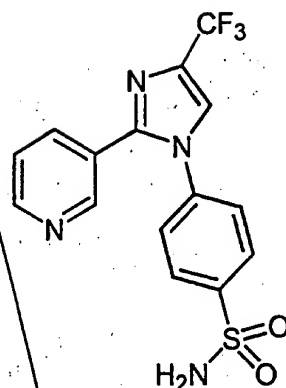
3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

TO500T-ES00860

See 1 a cont

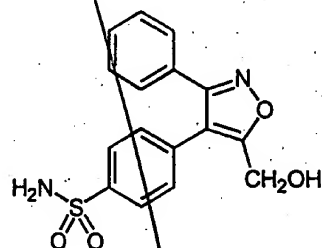
-329-

36)



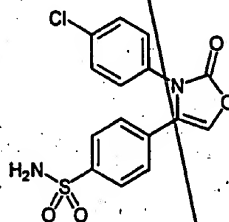
4-[2-(3-pyridinyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,

37)



4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

38)

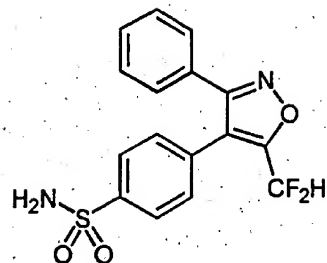


4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

Supp  
cont  
T05001-000000

-330-

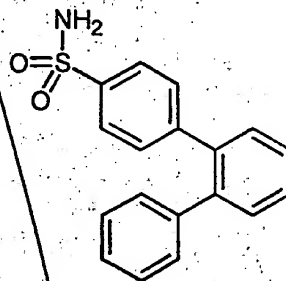
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

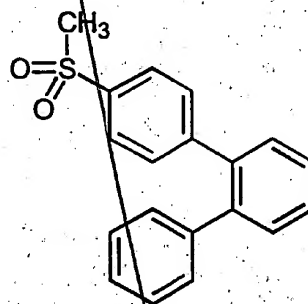
5

40)



[1,1':2',1''-terphenyl]-4-sulfonamide,

41)

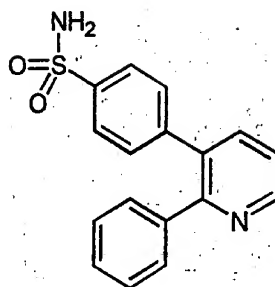


10

4-(methylsulfonyl)-1,1',2',1''-terphenyl,

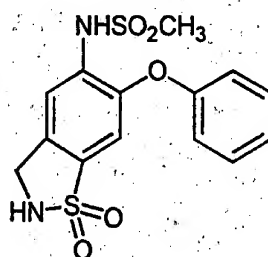
-331-

42)



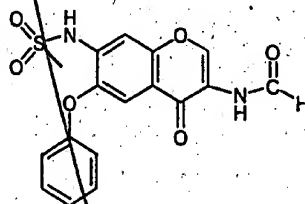
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)



N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

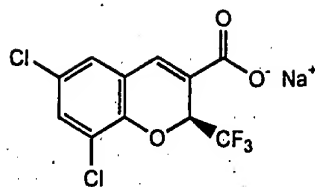
See  
a  
text

5

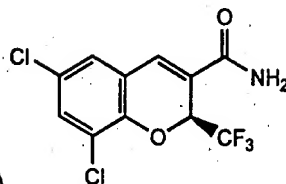
10

-332-

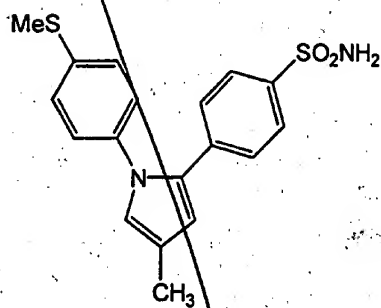
45)



46)

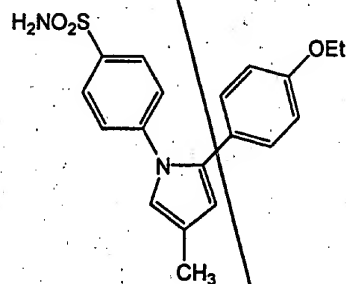


47)



, and

48)



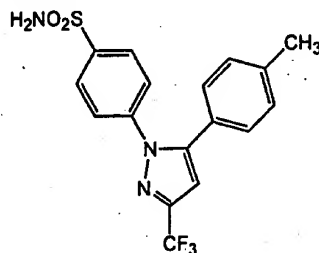
35. The method of Claim 1 wherein the  
 10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-  
 (methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

Suba  
 Cont  
 10500290860

-333-

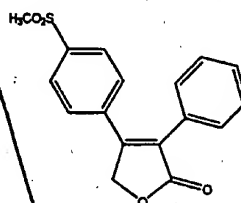
36. The method of Claim 1 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-(4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

37. The method of Claim 1 wherein the  
5 cyclooxygenase-2 inhibitor is



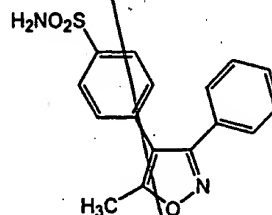
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

38. The method of Claim 1 wherein the  
10 cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

15            39. The method of Claim 1 wherein the  
cyclooxygenase-2 inhibitor is



4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

SECRET

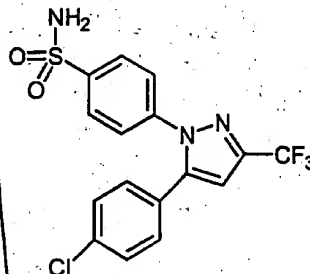
Sub: Art



-334-

40. The method of Claim 1 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

41. The method of Claim 1 wherein the  
5 cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

42. The method of Claim 1 wherein the neoplasia is  
10 selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

43. The method of Claim 1 wherein the neoplasia is  
15 selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenosarcoma, adenosquamous carcinoma, astrocytic tumors, bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma, carcinosarcoma,  
20 cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid, Ewing's sarcoma,  
25 fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma, glucagonoma,

09363005-109501

*Sub 1  
cont*

-335-

hemangiblastomas, hemangioendothelioma, hemangiomas,  
hepatic adenoma, hepatic adenomatosis, hepatocellular  
carcinoma, insulinoma, intraepithelial neoplasia,  
interepithelial squamous cell neoplasia, invasive  
5 squamous cell carcinoma, large cell carcinoma,  
leiomyosarcoma, lentigo maligna melanomas, malignant  
melanoma, malignant mesothelial tumors, medulloblastoma,  
medulloepithelioma, melanoma, meningeal, mesothelial,  
metastatic carcinoma, mucoepidermoid carcinoma,  
10 neuroblastoma, neuroepithelial adenocarcinoma nodular  
melanoma, oat cell carcinoma, oligodendroglial,  
osteosarcoma, pancreatic polypeptide, papillary serous  
adenocarcinoma, pineal cell, pituitary tumors,  
plasmacytoma, pseudosarcoma, pulmonary blastoma, renal  
15 cell carcinoma, retinoblastoma, rhabdomyosarcoma,  
sarcoma, serous carcinoma, small cell carcinoma, soft  
tissue carcinomas, somatostatin-secreting tumor,  
squamous carcinoma, squamous cell carcinoma,  
submesothelial, superficial spreading melanoma,  
20 undifferentiated carcinoma, uveal melanoma, verrucous  
carcinoma, vipoma, well differentiated carcinoma, and  
Wilm's tumor.

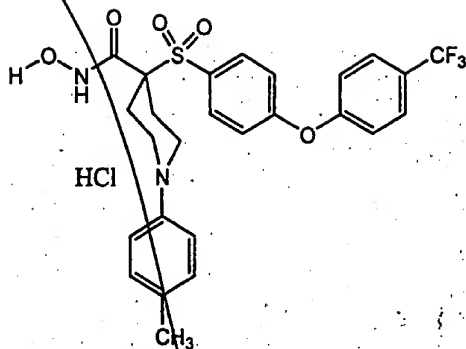
44. The method of Claim 1 wherein the matrix  
25 metalloproteinase inhibitor is selected from compounds,  
and their pharmaceutically acceptable salts thereof, of  
the group consisting of:

FOUO-10501

Suff  
Cont

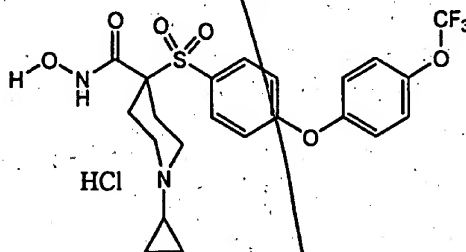
-336-

1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

2)

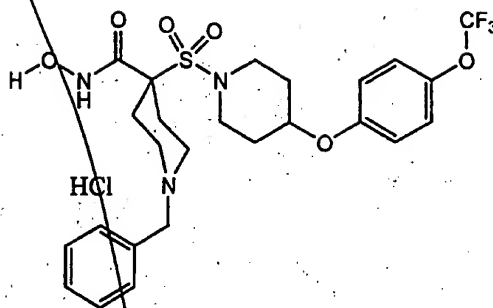


1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

Sub 1  
cont  
10503-10504

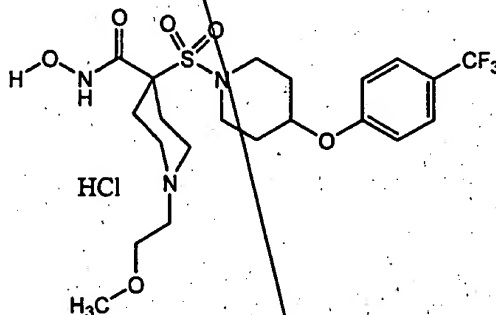
-337-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

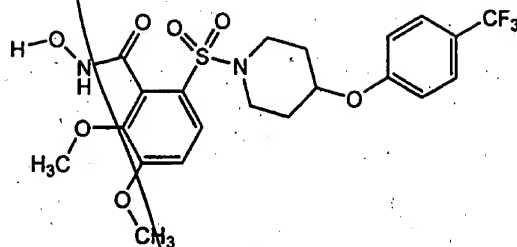


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

Suba Cont

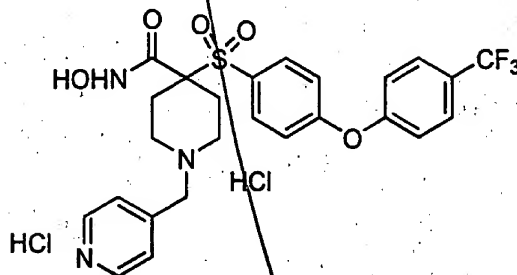
-338-

5)



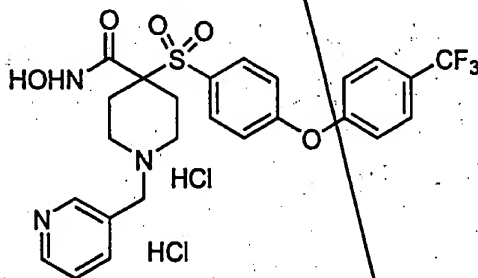
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide;

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)

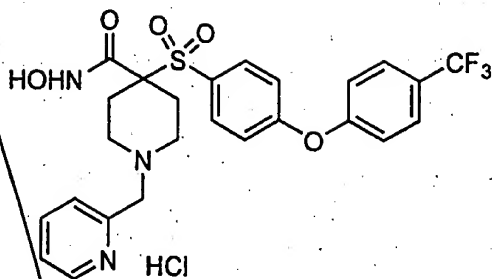


N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

FOUO 0001 2003 9360

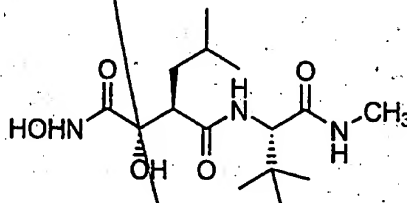
*See a Cont*

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)



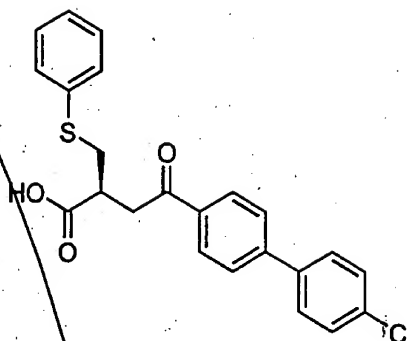
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*),2R\*,3S\*]]-),

~~0-9876543~~

Sub 1  
a  
cont

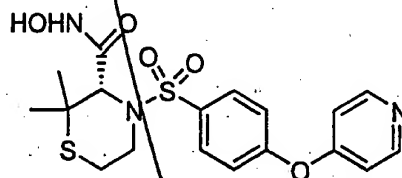
-340-

10}



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]- 4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2  
dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl] 3-  
thiomorpholinecarboxamide,

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),  
6-demethyl-6-deoxy-4-  
dedimethylaminotetracycline,

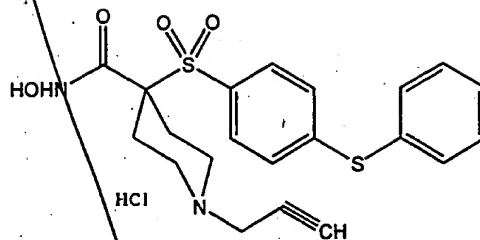
13) Chiroscience D-2163, 2- [1S- ([ (2R,S)-  
acetylmercapto- 5- phthalimido]pentanoyl- L-  
leucyl)amino- 3- methylbutyl]imidazole,

[illegible]

Sub a  
Don't

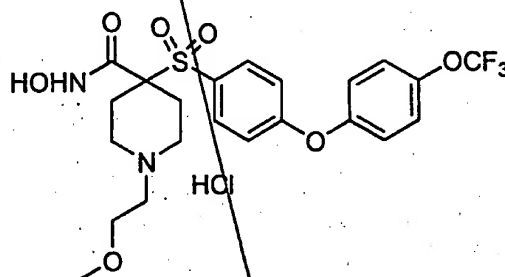
-341-

14)



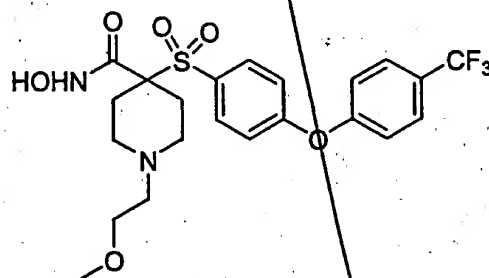
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-  
1-(2-propynyl)-4-piperidinecarboxamide  
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide monohydrochloride,

16)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide,

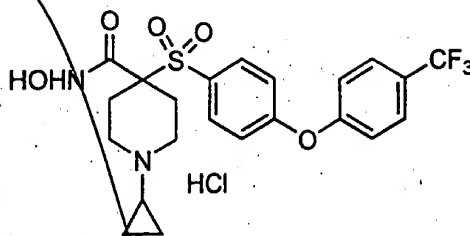
09868060100501

Suba!  
cont



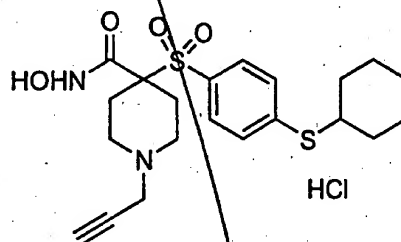
-342-

17)



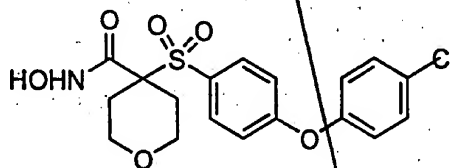
1-cyclopropyl-N-hydroxy-4-[[4-[(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)

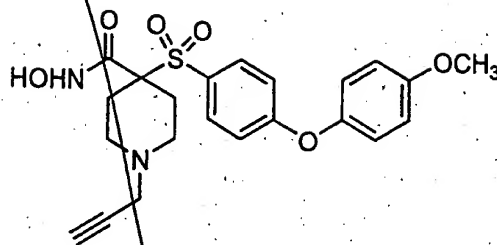


4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

098580001  
 T0500T-000985800  
 Sup a  
 Corit

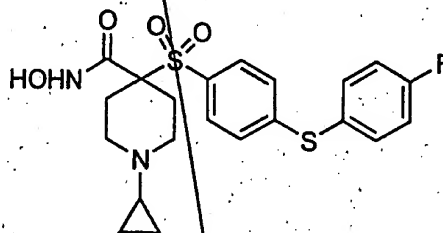
-343-

20)



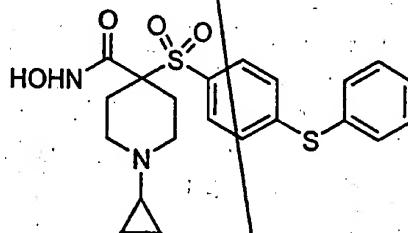
N-hydroxy-4-([4-(4-methoxyphenoxy)phenyl]sulfonyl)-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-([4-(4-fluorophenylthio)phenyl]sulfonyl)-N-hydroxy-4-piperidinecarboxamide,

22)

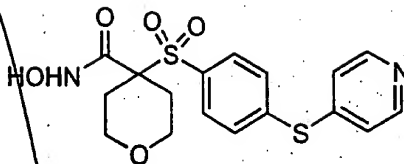


1-cyclopropyl-N-hydroxy-4-([4-(phenylthio)phenyl]sulfonyl)-4-piperidinecarboxamide,

TO5081-10089860  
Sub a cont

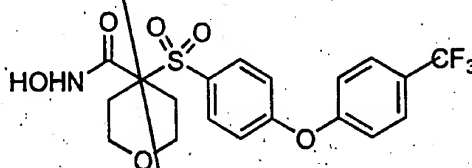
-344-

23)



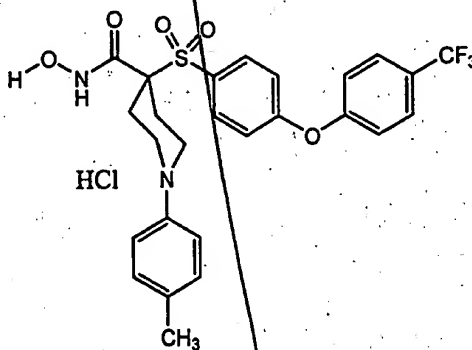
tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide and

24)



tetrahydro-N-hydroxy-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-2H-pyran-4-carboxamide.

45. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is

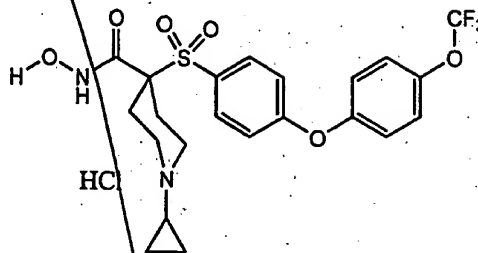


N-hydroxy-1-(4-methylphenyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

09863061-100501  
 Sub, a  
 Cont

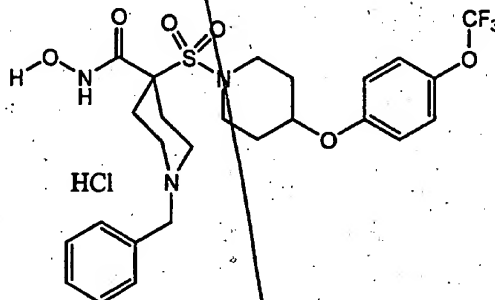
-345-

46. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

47. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is

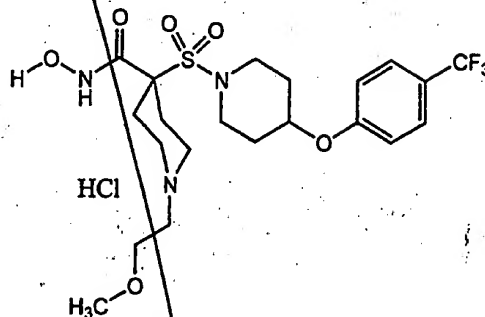


N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

Sub a  
cont

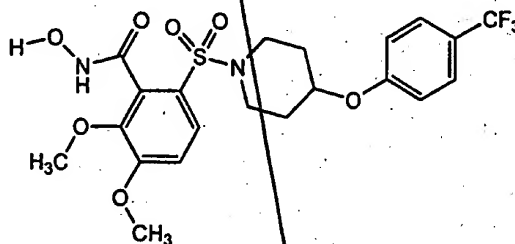
-346-

48. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

49. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is

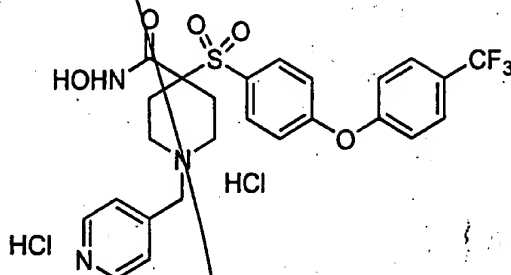


10 N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

10500100501

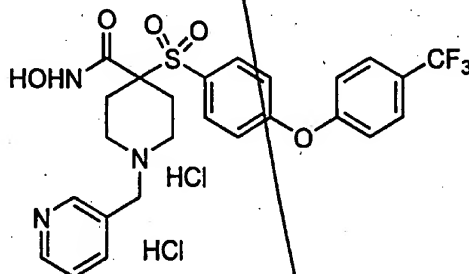
*Sub 1 Cont*

50. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

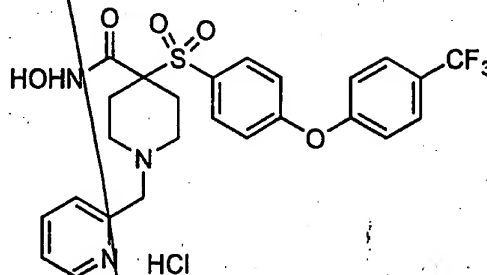
51. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



15 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

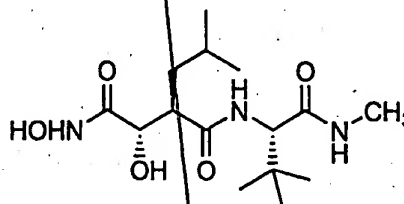
-348-

52. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

53. The method of Claim 1 wherein the matrix  
10 metalloproteinase inhibitor is



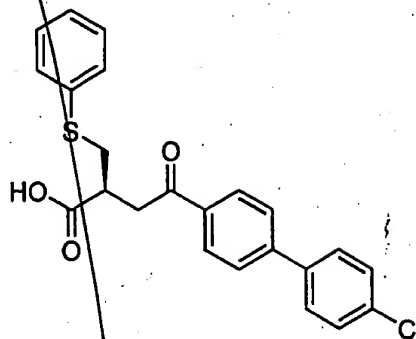
15 British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*), 2R\*, 3S\*]]-).

0986000100009860

Sub 1  
Out

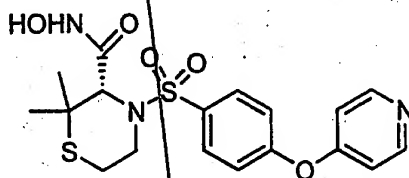
-349-

54. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]-4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid.

55. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is



15 Agouron Pharmaceuticals AG-3340, N-hydroxy-  
2,2-dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl]-3-  
thiomorpholinecarboxamide.

56. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is CollaGenex  
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-  
20 dedimethylaminotetracycline..

TO SUE 1-1-99 093560

Sub 1  
Cont



-350-

57. The method of Claim 1 wherein the matrix metalloproteinase inhibitor is Chiroscience D-2163, 2-[1S- ((2R,S)- acetylmercapto- 5- phthalimido]pentanoyl-L-leucyl)amino- 3- methylbutyl]imidazole.

5

58. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of radiation, a cyclooxygenase-2 inhibitor, a matrix metalloproteinase inhibitor, and an antineoplastic agent, wherein said antineoplastic agent is selected from the group consisting of anastrozole, calcium carbonate, capecitabine, carboplatin, cisplatin, Cell Pathways CP-461, docetaxel, doxorubicin, etoposide, fluorouracil (5-FU), fluoxymestrine, gemcitabine, goserelin, irinotecan, ketoconazole, letrozol, leucovorin, levamisole, megestrol, mitoxantrone, paclitaxel, raloxifene, retinoic acid, tamoxifen, thiotepa, topotecan, toremifene, vinorelbine, vinblastine, vincristine, selenium (selenomethionine), ursodeoxycholic acid, sulindac sulfone, exemestane and eflornithine (DFMO).

10

15

20

25

59. The method of Claim 58 wherein the combination is administered in a sequential manner.

60. The method of Claim 58 wherein the combination is administered in a substantially simultaneous manner.

30

SUBMITTED TO THE USPTO

Sub 1  
Ont

-351-

61. The method of Claim 58 wherein the antineoplastic agent is capecitabine.

62. The method of Claim 58 wherein the  
5 antineoplastic agent is carboplatin.

63. The method of Claim 58 wherein the antineoplastic agent is cisplatin.

10            64. The method of Claim 58 wherein the  
              antineoplastic agent is Cell Pathways CP-461.

65. The method of Claim 58 wherein the antineoplastic agent is docetaxel.

66. The method of Claim 58 wherein the antineoplastic agent is doxorubicin.

67. The method of Claim 58 wherein the  
20 antineoplastic agent is etoposide.

68. The method of Claim 58 wherein the antineoplastic agent is fluoxymestrine.

25 69. The method of Claim 58 wherein the  
antineoplastic agent is gemcitabine.

70. The method of Claim 58 wherein the antineoplastic agent is goserelin.

71. The method of Claim 58 wherein the antineoplastic agent is irinotecan.

72. The method of Claim 58 wherein the antineoplastic agent is ketoconazole.

5 73. The method of Claim 58 wherein the antineoplastic agent is letrozol.

74. The method of Claim 58 wherein the antineoplastic agent is leucovorin.

10 75. The method of Claim 58 wherein the antineoplastic agent is levamisole.

15 76. The method of Claim 58 wherein the antineoplastic agent is megestrol.

77. The method of Claim 58 wherein the antineoplastic agent is mitoxantrone.

20 78. The method of Claim 58 wherein the antineoplastic agent is paclitaxel.

79. The method of Claim 58 wherein the antineoplastic agent is raloxifene.

25 80. The method of Claim 58 wherein the antineoplastic agent is retinoic acid.

30 81. The method of Claim 58 wherein the antineoplastic agent is tamoxifen

005001300

Sub  
cont

-353-

82. The method of Claim 58 wherein the antineoplastic agent is thiotepa.

83. The method of Claim 58 wherein the antineoplastic agent is topotecan.

84. The method of Claim 58 wherein the antineoplastic agent is toremifene.

10 85. The method of Claim 58 wherein the antineoplastic agent is vinorelbine.

15 86. The method of Claim 58 wherein the antineoplastic agent is vinblastine.

87. The method of Claim 58 wherein the antineoplastic agent is vincristine.

20 88. The method of Claim 58 wherein the antineoplastic agent is selenium (selenomethionine).

89. The method of Claim 58 wherein the antineoplastic agent is sulindac sulfone.

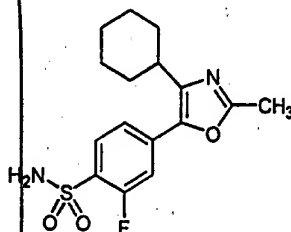
25 90. The method of Claim 58 wherein the antineoplastic agent is eflornithine (DFMO).

Sub 1  
cont  
"10501"

-354-

91. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

5                      1)



JTE-522, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-  
2-fluorobenzenesulfonamide,

2)

10

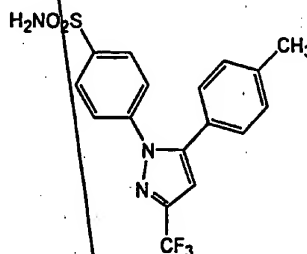
5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,

3)

2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

15

4)

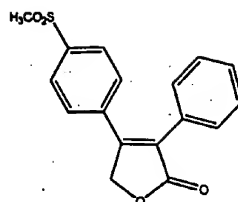


4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide,

Sub Cont

-355-

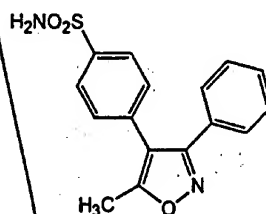
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone,

5

6)



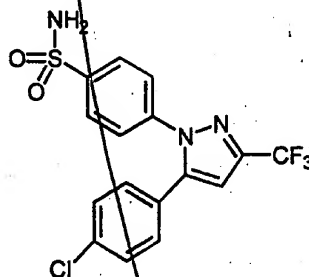
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

7)

N-[[4-(5-methyl-3-phenylisoxazol-4yl)phenyl]sulfonyl]propanamide,

10

8)

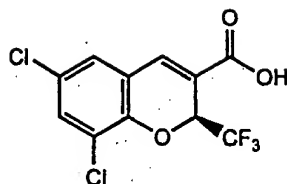


4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide,

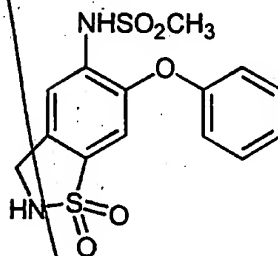
09860001 E000000000  
Sub a  
cont

-356-

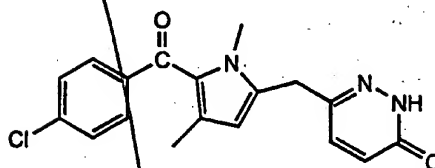
9)



10)

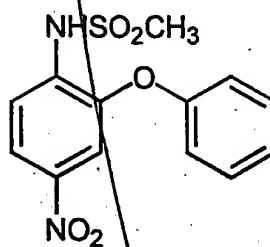


11)



6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

12)

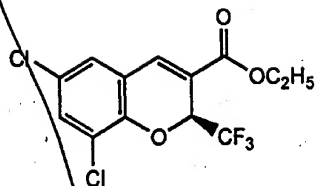


N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

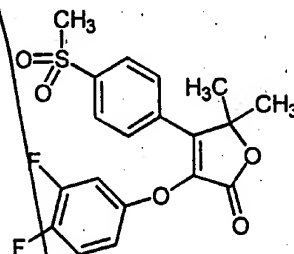
Supp. Cont  
T0500T-99000000

-357-

13)

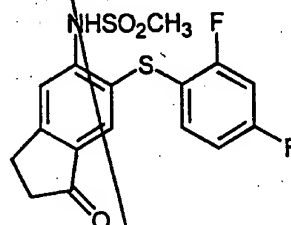


14)



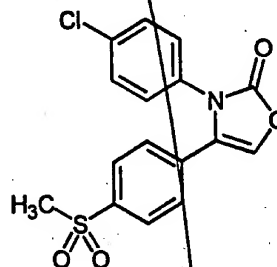
3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

15)



N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

16)



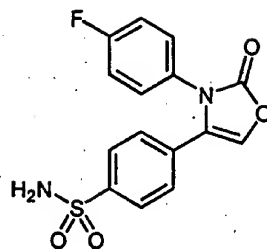
3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

Sub a cont



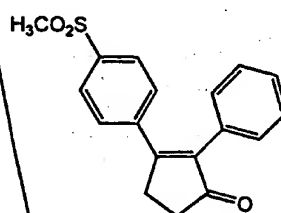
-358-

17)



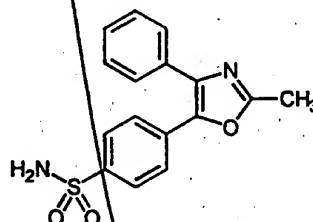
4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



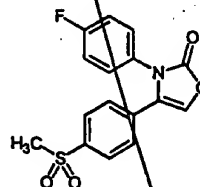
3-[4-(methanesulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

19)



4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

20)

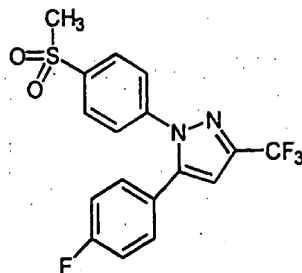


3-(4-fluorophenyl)-4-[4-(methanesulfonyl)phenyl]-2(3H)-oxazolone,

Suppl  
Cont

-359-

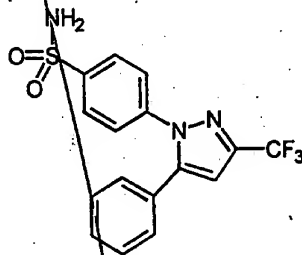
21)



5- (4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

5

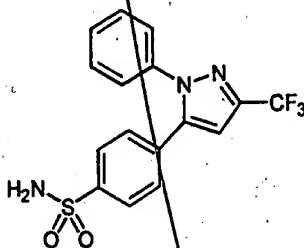
22)



4-[5-phenyl]-3-(trifluoromethyl)-1H-pyrazol-1-yl benzenesulfonamide,

10

23)



4-[1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5-yl] benzenesulfonamide,

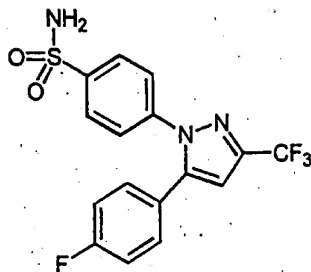
15

09868066 100501

Sub 1  
Cont

-360-

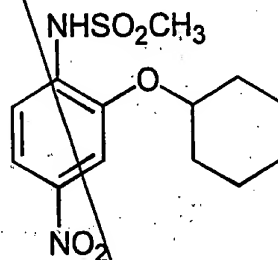
24)



4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

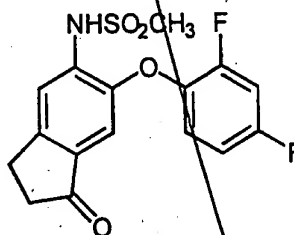
5

25)



N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

26)



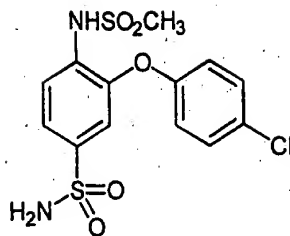
N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

10

Supp  
Cont

-361-

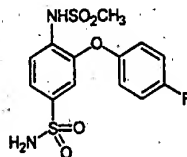
27)



3-(4-chlorophenoxy)-4-  
[(methylsulfonyl)amino]benzenesulfonamide,

5

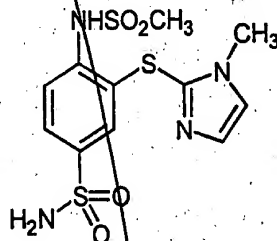
28)



3-(4-fluorophenoxy)-4-  
[(methylsulfonyl)amino]benzenesulfonamide,

10

29)

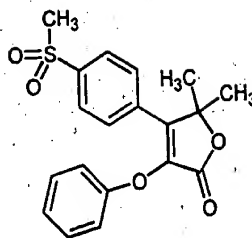


3-[(1-methyl-1H-imidazol-2-yl)thio]-4-  
[(methylsulfonyl) amino]benzenesulfonamide,

TO500T-5909860

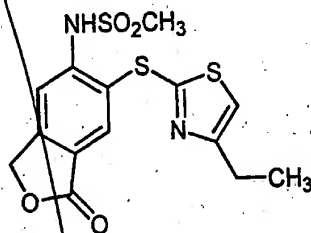
Sub  
cont

30)



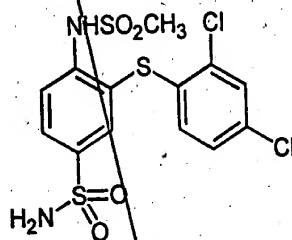
5

31)



10

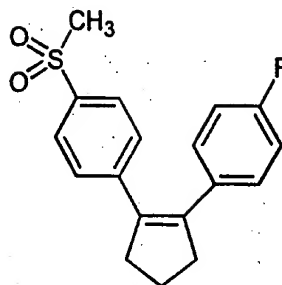
32)



3-[(2,4-dichlorophenyl)thio]-4-  
[(methylsulfonyl)amino]benzenesulfonamide,

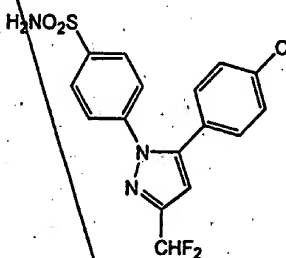
-363-

33)



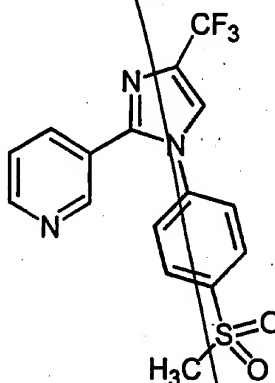
1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,

34)



4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

35)



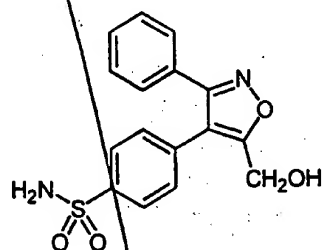
3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

Sub, a Cont  
0456063:100504

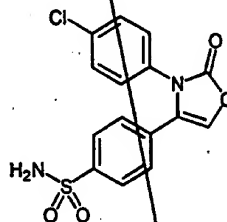
-364-

Nc1ccc(cc1n1c2cc(C(F)(F)F)cn2-c2ccncc2)S(=O)(=O)c3ccccc3

37)



38)



4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

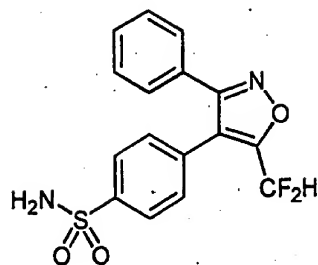
10

THE UNIVERSITY OF CHICAGO

Suba  
cont

-365-

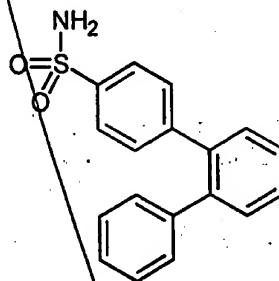
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

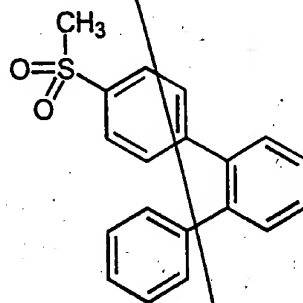
5

40)



[1,1':2',1''-terphenyl]-4-sulfonamide,

41)



10

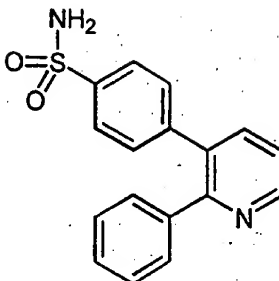
4-(methylsulfonyl)-1,1',2',1''-terphenyl,

Sub  
Cont



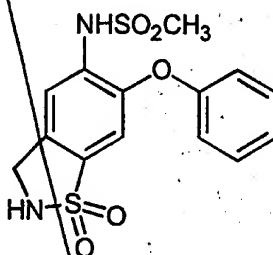
-366-

42)



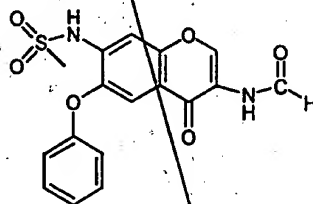
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)



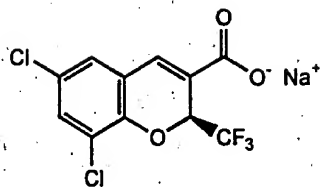
10.

N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

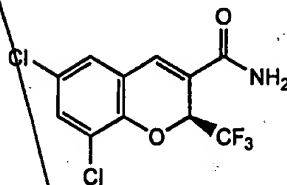
*Suzanne Cont*

-367-

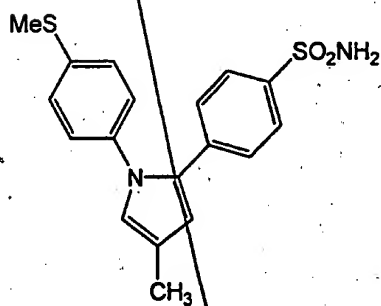
45)



46)

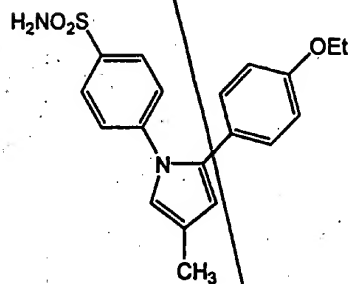


47)



and

48)

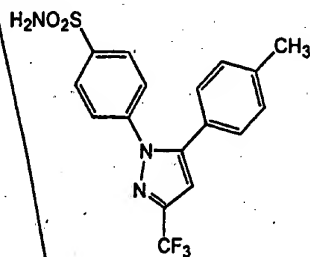


92. The method of Claim 58 wherein the  
10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-  
(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

-368-

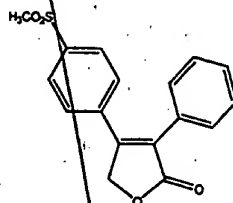
93. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

94. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



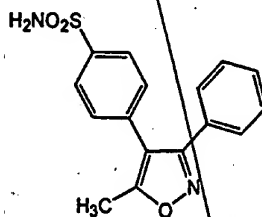
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

95. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

96. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is



4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

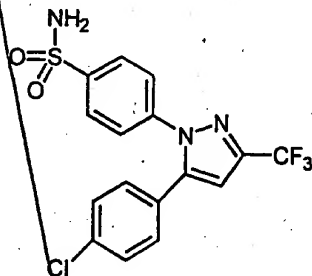
T05007-2008-03-05

*Sub a  
not*

-369-

97. The method of Claim 58 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

98. The method of Claim 58 wherein the  
5 cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

99. The method of Claim 58 wherein the neoplasia  
10 is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

100. The method of Claim 58 wherein the neoplasia  
is selected from the group consisting of acral  
15 lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenocarcinoma, adenosquamous carcinoma, astrocytic tumors, Bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma,  
20 carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epitheloid,  
25 Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma,

0936303-100501  
 Sub 1  
 cont

-370-

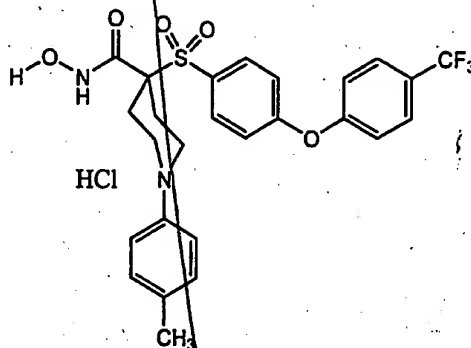
- glucagonoma, hemangiblastomas, hemangioendothelioma,  
hemangiomas, hepatic adenoma, hepatic adenomatosis,  
hepatocellular carcinoma, insulinoma, intraepithelial  
neoplasia, interepithelial squamous cell neoplasia,  
5 invasive squamous cell carcinoma, large cell carcinoma,  
leiomyosarcoma, lentigo maligna melanomas, malignant  
melanoma, malignant mesothelial tumors, medulloblastoma,  
medulloepithelioma, melanoma, meningeal, mesothelial,  
metastatic carcinoma, mucoepidermoid carcinoma,  
10 neuroblastoma, neuroepithelial adenocarcinoma nodular  
melanoma, oat cell carcinoma, oligodendroglial,  
osteosarcoma, pancreatic polypeptide, papillary serous  
adenocarcinoma, pineal cell, pituitary tumors,  
plasmacytoma, pseudosarcoma, pulmonary blastoma, renal  
15 cell carcinoma, retinoblastoma, rhabdomyosarcoma,  
sarcoma, serous carcinoma, small cell carcinoma, soft  
tissue carcinomas, somatostatin-secreting tumor,  
squamous carcinoma, squamous cell carcinoma,  
submesothelial, superficial spreading melanoma,  
20 undifferentiated carcinoma, uveal melanoma, verrucous  
carcinoma, vipoma, well differentiated carcinoma, and  
Wilm's tumor.

Sub 1  
100504  
TOSOT-ESOT

-371-

101. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

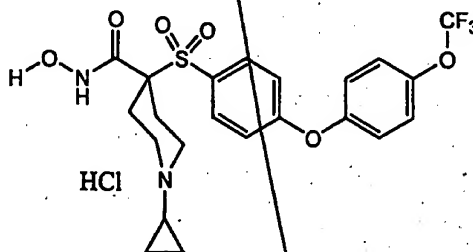
5 1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

10

2)



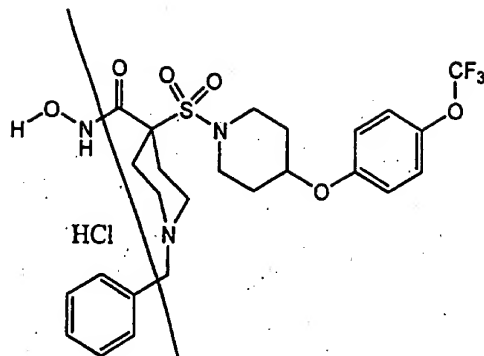
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

15

subd  
cont  
105007-10501

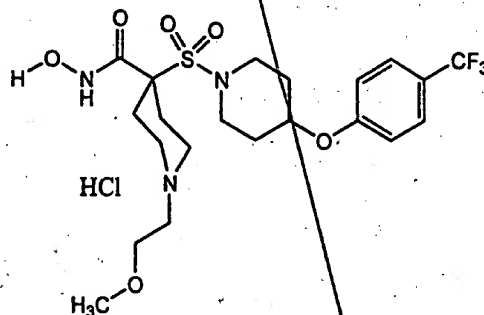
-372-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

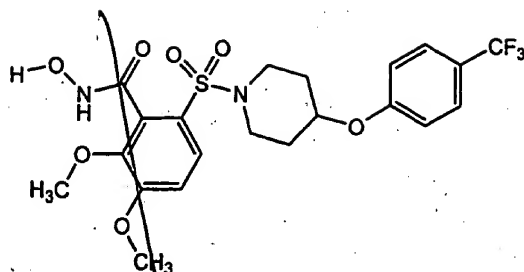


N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

098663100501  
Saxa  
Cont

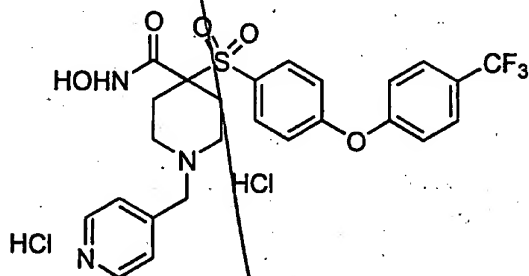
-373-

5)



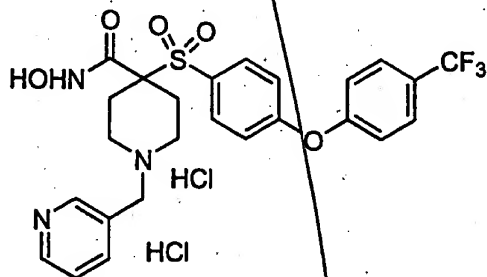
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



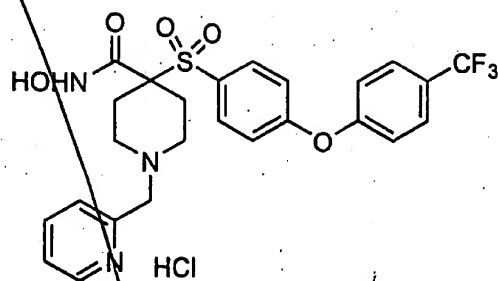
N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

Sub a  
Unit



-374-

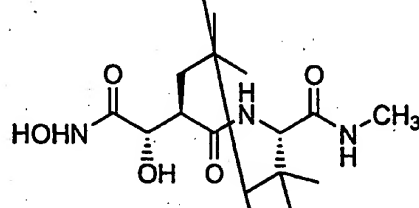
8)



5

N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)



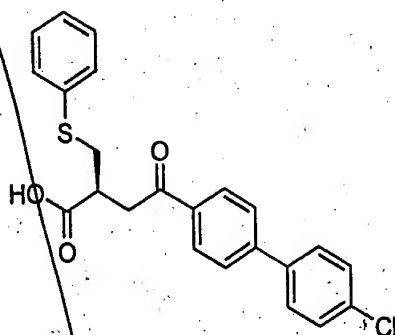
10

British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3-(2-methylpropyl)-, [2S-[N4(R\*),2R\*,3S\*]]-,

Suba  
Ent  
TOSOT-2003-100501

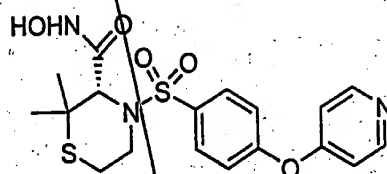
-375-

10)



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]- 4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2  
dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl] 3-  
thiomorpholinecarboxamide,

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),  
6-demethyl-6-deoxy-4-  
dedimethylaminotetracycline,

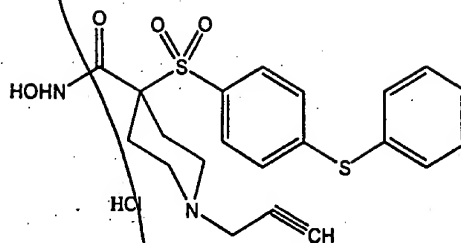
13) Chiroscience D-2163, 2- [1S- ((2R,S)-  
acetylmercapto- 5- phthalimido]pentanoyl- L-  
leucyl)amino- 3- methylbutyl]imidazole,

TOC00159939360

Sub 1  
cont

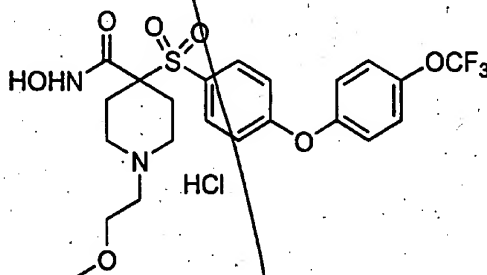
-376-

14)



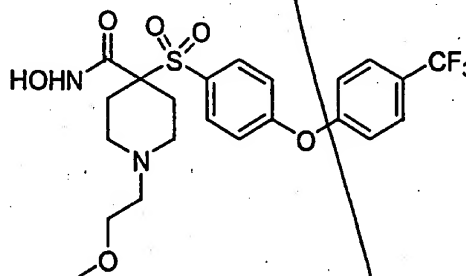
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-  
1-(2-propynyl)-4-piperidinecarboxamide  
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

16)

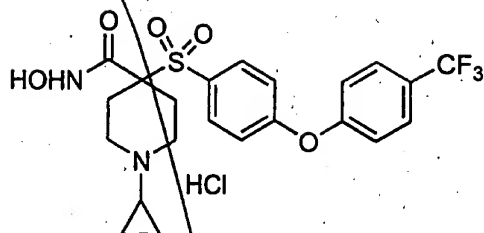


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide,

105001-20039860  
 See a Cont

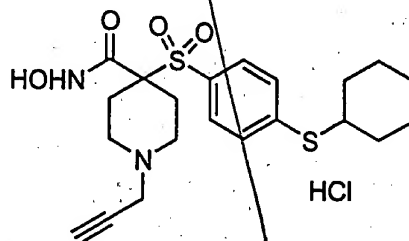
-377-

17)



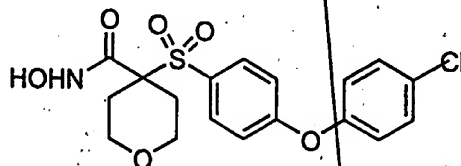
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)



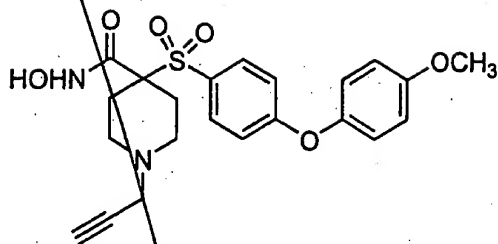
4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

TO5001-1008860

Sub a  
cont

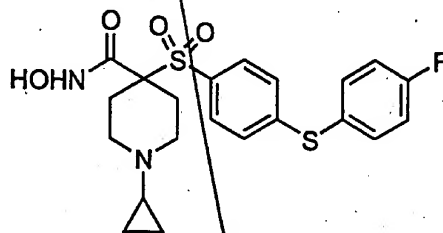
-378-

20)



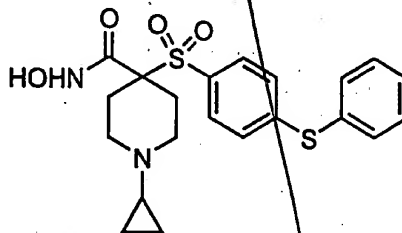
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl]sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)

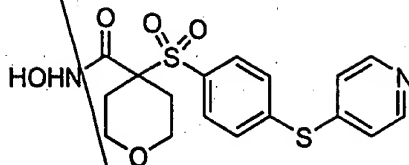


1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

09863007-10504  
Sub a' Cont

-379-

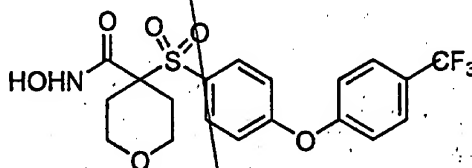
23)



tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

5

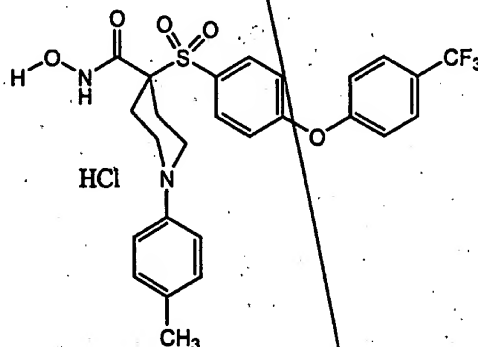
24)



tetrahydro-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-pyran-4-carboxamide.

10

102. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



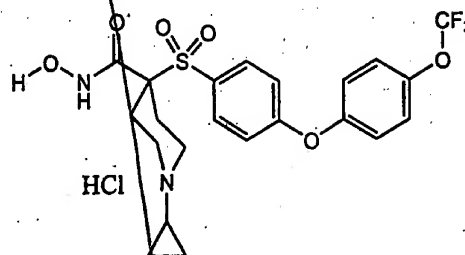
N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

15

09863030.100501  
 Sub a  
 Cont

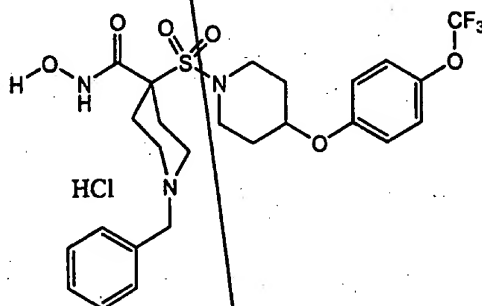
-380-

103. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

104. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



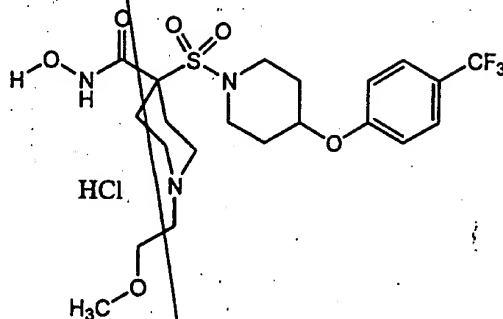
N-hydroxy-1-(phenylmethyl)-4-[[4-[(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

09863063100001

*See Cont*

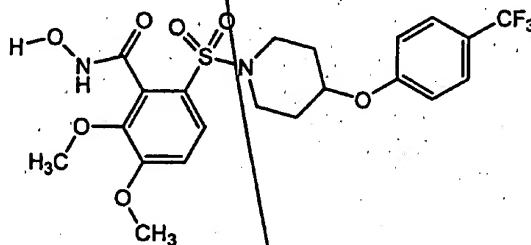
-381-

105. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

106. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



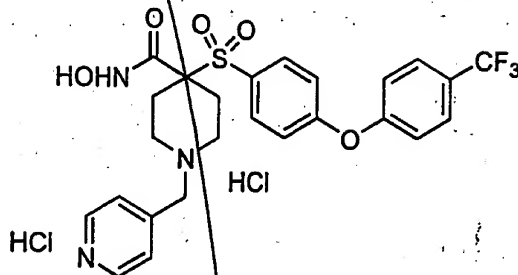
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

Sub 1 cont



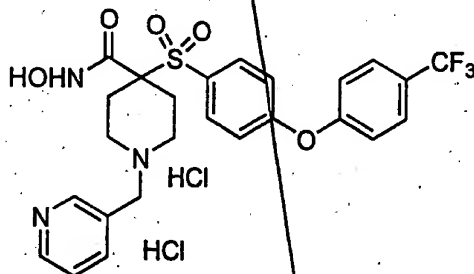
-382-

107. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

108. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

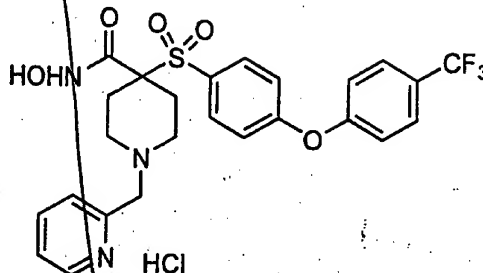


15 N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

Suba cont

-383-

109. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

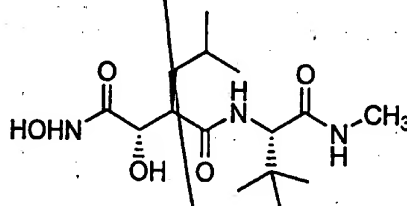


5

N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

110. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is

10



15

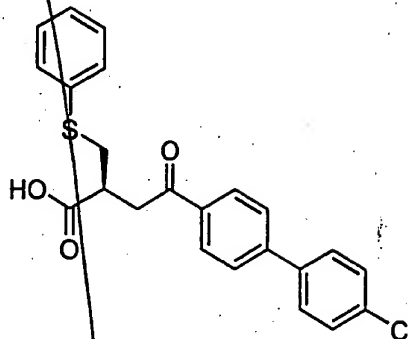
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*), 2R\*, 3S\*]]-).

09863000-100501

Supp 1  
cont

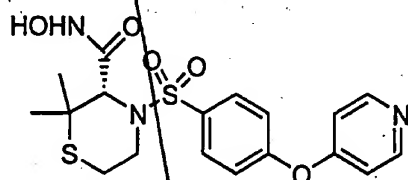
-384-

111. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]-4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid.

112. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is



10 Agouron Pharmaceuticals AG-3340, N-hydroxy-  
2,2-dimethyl-4-[[4-(4-  
15 pyridinyloxy)phenyl]sulfonyl]-3-  
thiomorpholinecarboxamide.

113. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is CollaGenex  
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-  
20 dedimethylaminotetracycline.

114. The method of Claim 58 wherein the matrix metalloproteinase inhibitor is Chiroscience D-2163, 2-

0986800-10501

Sub a  
Cont

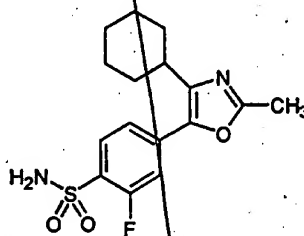
-385-

[1S- ((2R,S)- acetylmercapto- 5- phthalimido]pentanoyl-  
L- leucyl)amino- 3- methylbutyl]imidazole.

115. A combination comprising a cyclooxygenase-2  
5 inhibitor, a matrix metalloproteinase inhibitor, and an  
antineoplastic agent, wherein said antineoplastic agent  
is selected from the group consisting of anastrozole,  
calcium carbonate, capecitabine, carboplatin, cisplatin,  
Cell Pathways CP-461, docetaxel, doxorubicin, etoposide,  
10 fluorouracil (5-FU), fluoxymestrine, gemcitabine,  
goserelin, irinotecan, ketoconazole, letrozol,  
leucovorin, levamisole, megestrol, mitoxantrone,  
paclitaxel, raloxifene, retinoic acid, tamoxifen,  
thiotepa, topotecan, toremifene, vinorelbine,  
15 vinblastine, vincristine, selenium (selenomethionine),  
ursodeoxycholic acid, sulindac sulfone, exemestane and  
eflornithine (DFMO).

116. The combination of Claim 115 wherein the  
20 cyclooxygenase-2 inhibitor is selected from compounds,  
and their pharmaceutically acceptable salts thereof, of  
the group consisting of:

1)



25 JTE-522, 4-(4-cyclohexyl-2-methyloxazol-5-yl)-  
2-fluorobenzenesulfonamide,

09660001-10089860

*Sub a  
cont*

-386-

2)

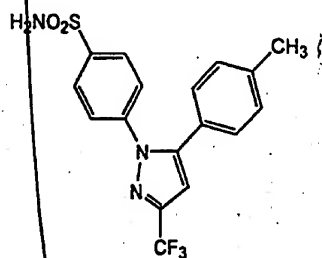
5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine,

3)

5

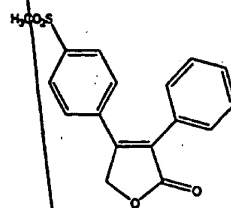
2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one,

4)



4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide,

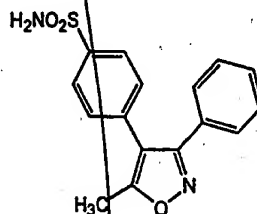
5)



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone,

6)

15



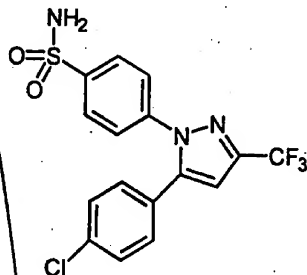
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide,

098600-10501  
 TOSOT-1009860  
 Sup a cont

-387-

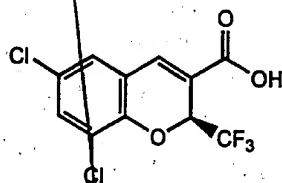
- 7) N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide,

8)

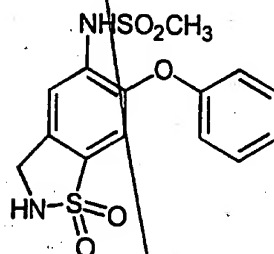


- 4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

9)

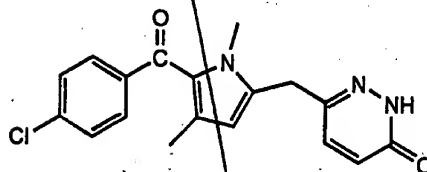


- 10)



10.

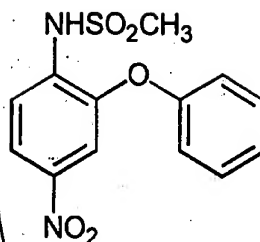
- 11)



- 6-[[5-(4-chlorobenzoyl)-1,4-dimethyl-1H-pyrrol-2-yl]methyl]-3(2H)-pyridazinone,

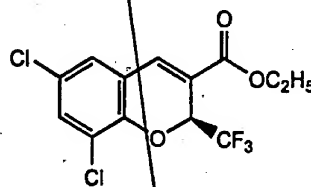
-388-

12)

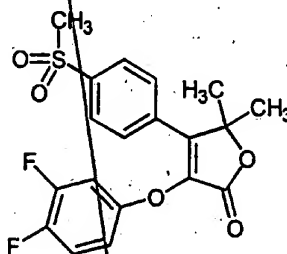


N-(4-nitro-2-phenoxyphenyl)methanesulfonamide,

13)

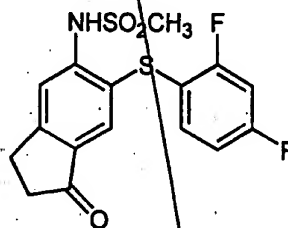


14)



3-(3,4-difluorophenoxy)-5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-2(5H)-furanone,

15)

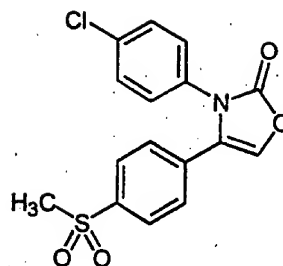


N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

Sub 1  
Cont

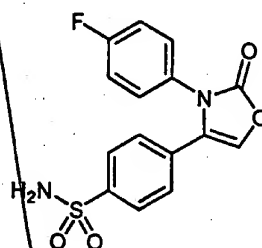
-389-

16)



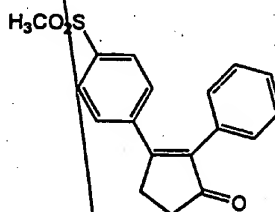
3-(4-chlorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

5 17)



4-[3-(4-fluorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

18)



3-[4-(methanesulfonyl)phenyl]-2-phenyl-2-cyclopenten-1-one,

10

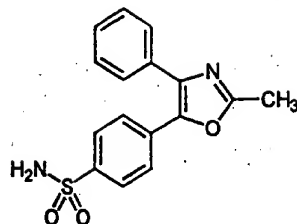
TOCSET 20000000

Suba!  
cont



-390-

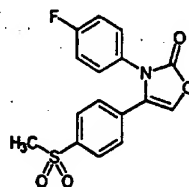
19)



4-(2-methyl-4-phenyl-5-oxazolyl)benzenesulfonamide,

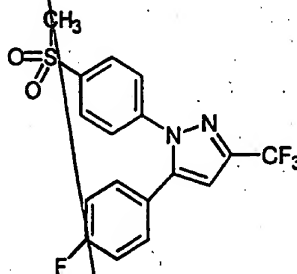
5

20)



3-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2(3H)-oxazolone,

21)



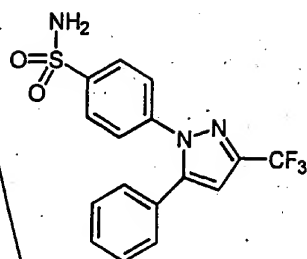
10

5-(4-fluorophenyl)-1-[4-(methylsulfonyl)phenyl]-3-(trifluoromethyl)-1H-pyrazole,

098600610001  
 T00001E9089860

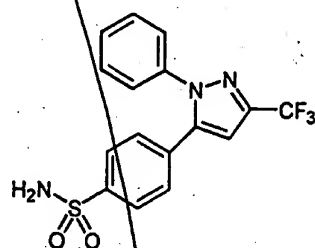
Suba  
cont

22)

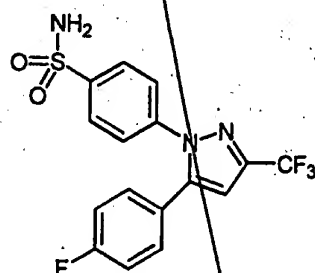


5

23)



24)



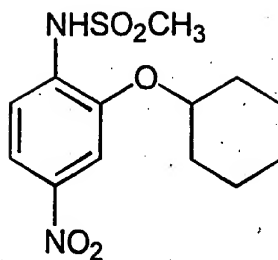
4-[5-(4-fluorophenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

10

Suba<sup>1</sup> Cent

-392-

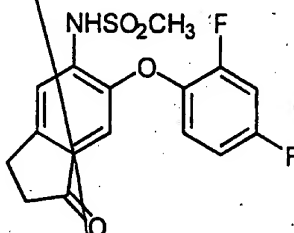
25)



N-[2-(cyclohexyloxy)-4-nitrophenyl]methanesulfonamide,

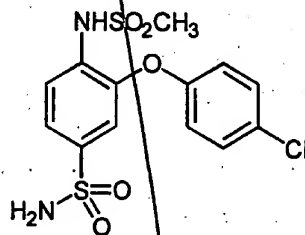
5

26)



N-[6-(2,4-difluorophenoxy)-2,3-dihydro-1-oxo-1H-inden-5-yl]methanesulfonamide,

27)



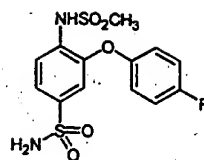
3-(4-chlorophenoxy)-4-[(methylsulfonyl)amino]benzenesulfonamide,

10

TO5001-1233360  
Sub 1  
Cont

-393-

28)

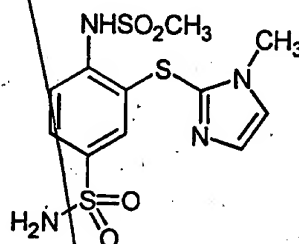


3-(4-fluorophenoxy)-4-

[(methylsulfonyl)amino]benzenesulfonamide,

5

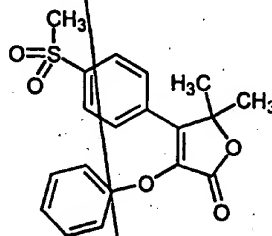
29)



3-[(1-methyl-1H-imidazol-2-yl)thio]-4

[(methylsulfonyl)amino]benzenesulfonamide,

30)



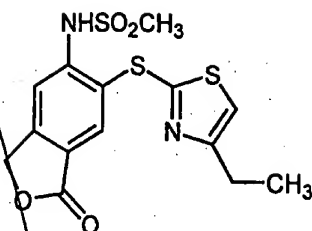
5,5-dimethyl-4-[4-(methylsulfonyl)phenyl]-3-phenoxy-2(5H)-furanone,

10

Supp  
Cont

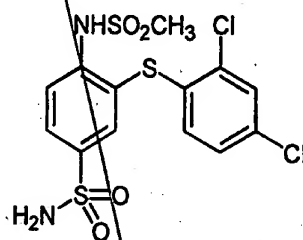
-394-

31)



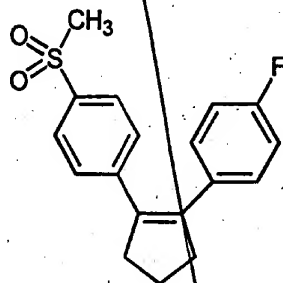
N-[6-[(4-ethyl-2-thiazolyl)thio]-1,3-dihydro-1-oxo-5-isobenzofuranyl]methanesulfonamide,

32)



3-[(2,4-dichlorophenyl)thio]-4-[(methylsulfonyl)amino]benzenesulfonamide,

33)



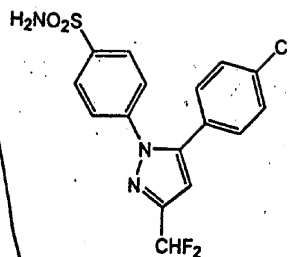
1-fluoro-4-[2-[4-(methylsulfonyl)phenyl]cyclopenten-1-yl]benzene,

09668063100501

Sub a  
Cont

-395-

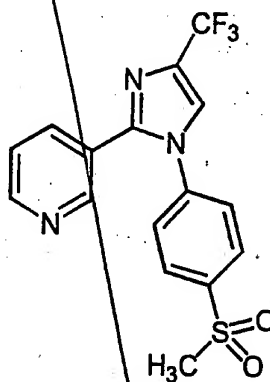
34)



4-[5-(4-chlorophenyl)-3-(difluoromethyl)-1H-pyrazol-1-yl]benzenesulfonamide,

5

35)

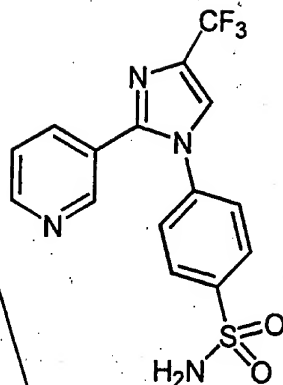


3-[1-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-1H-imidazol-2-yl]pyridine,

Supp.  
Cont

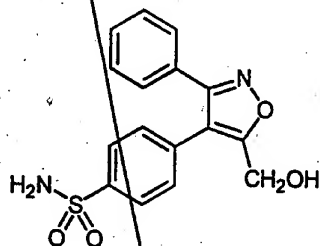
-396-

36)



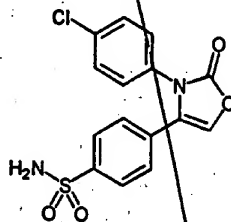
4-[2-(3-pyridinyl)-4-(trifluoromethyl)-1H-imidazol-1-yl]benzenesulfonamide,

37)



4-[5-(hydroxymethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

38)



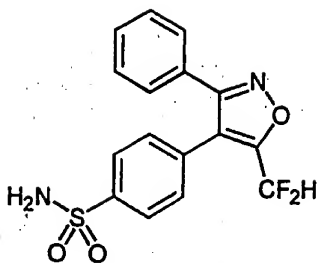
4-[3-(4-chlorophenyl)-2,3-dihydro-2-oxo-4-oxazolyl]benzenesulfonamide,

TO500T-10501

Sub A  
Cent

-397-

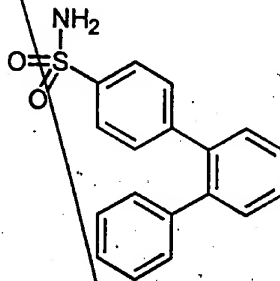
39)



4-[5-(difluoromethyl)-3-phenylisoxazol-4-yl]benzenesulfonamide,

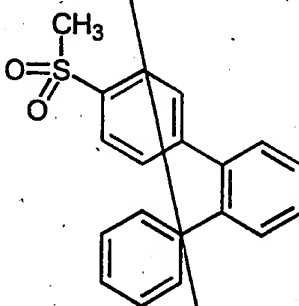
5

40)



[1,1':2',1''-terphenyl]-4-sulfonamide,

41)



4-(methylsulfonyl)-1,1',2,1''-terphenyl,

10

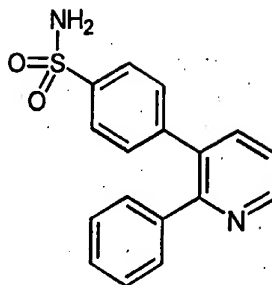
09868063-10504

*Sub 1  
Cont*



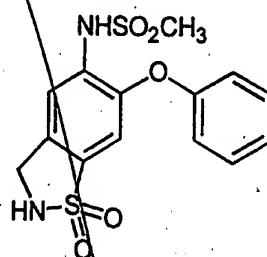
-398-

42)



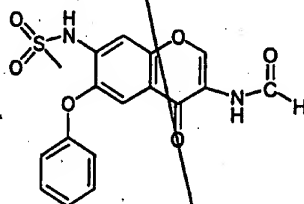
4-(2-phenyl-3-pyridinyl)benzenesulfonamide,

43)



N-(2,3-dihydro-1,1-dioxido-6-phenoxy-1,2-benzisothiazol-5-yl)methanesulfonamide, and

44)



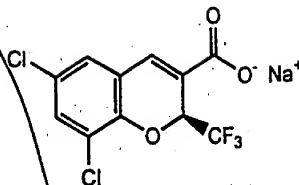
N-[3-(formylamino)-4-oxo-6-phenoxy-4H-1-benzopyran-7-yl]methanesulfonamide,

Sub a!  
Cont

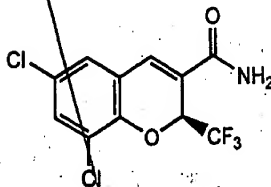
10

-399-

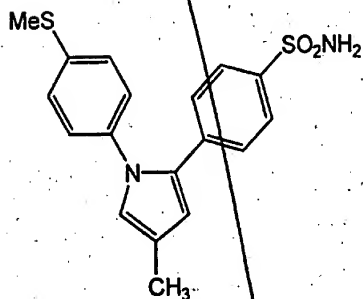
45)



46)

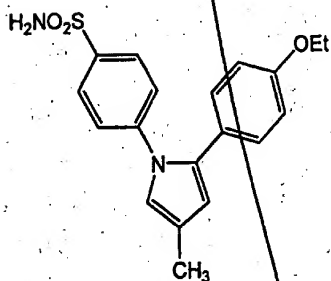


47)



, and

48)



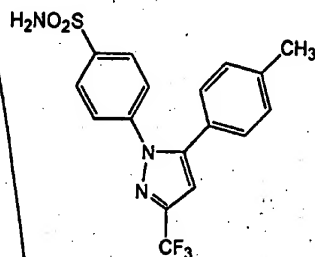
117. The combination of Claim 115 wherein the  
 10 cyclooxygenase-2 inhibitor is 5-chloro-3-(4-(methylsulfonyl)phenyl)-2-(methyl-5-pyridinyl)pyridine.

See  
 Cont

-400-

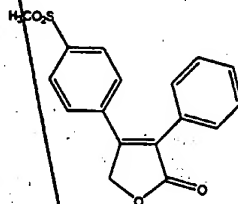
118. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is 2-(3,5-difluorophenyl)-3-4-(methylsulfonyl)phenyl)-2-cyclopenten-1-one.

119. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is



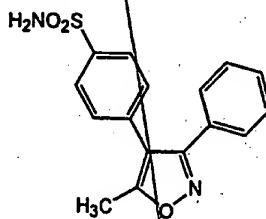
4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]-benzenesulfonamide.

120. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is



rofecoxib, 4-(4-(methylsulfonyl)phenyl)-3-phenyl-2(5H)-furanone.

121. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is



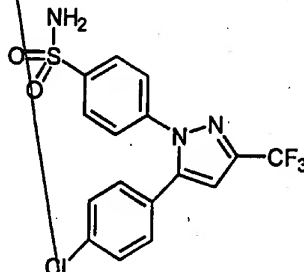
4-(5-methyl-3-phenylisoxazol-4-yl)benzenesulfonamide.

098800-100501  
 Sub a  
 Cont

-401-

122. The combination of Claim 115 wherein the cyclooxygenase-2 inhibitor is N-[[4-(5-methyl-3-phenylisoxazol-4-yl)phenyl]sulfonyl]propanamide.

123. The combination of Claim 115 wherein the  
5 cyclooxygenase-2 inhibitor is



4-[5-(4-chlorophenyl)-3-(trifluoromethyl)-1H-pyrazole-1-yl]benzenesulfonamide.

124. The combination of Claim 115 wherein the  
10 neoplasia is selected from the group consisting of lung cancer, breast cancer, gastrointestinal cancer, bladder cancer, head and neck cancer and cervical cancer.

125. The combination of Claim 115 wherein the  
15 neoplasia is selected from the group consisting of acral lentiginous melanoma, actinic keratoses, adenocarcinoma, adenoid cystic carcinoma, adenomas, adenocarcinoma, adenosquamous carcinoma, astrocytic tumors, Bartholin gland carcinoma, basal cell carcinoma, bronchial gland carcinomas, capillary, carcinoids, carcinoma,  
20 carcinosarcoma, cavernous, cholangiocarcinoma, chondrosarcoma, choroid plexus papilloma/carcinoma, clear cell carcinoma, cystadenoma, endodermal sinus tumor, endometrial hyperplasia, endometrial stromal sarcoma, endometrioid adenocarcinoma, ependymal, epithelioid,  
25 Ewing's sarcoma, fibrolamellar, focal nodular hyperplasia, gastrinoma, germ cell tumors, glioblastoma,

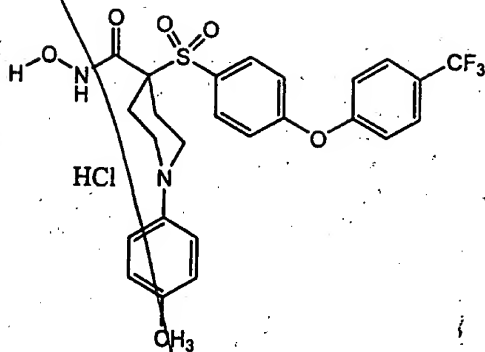
09862053100501  
Suba  
Cont

glucagonoma, hemangiblastomas, hemangioendothelioma, hemangiomas, hepatic adenoma, hepatic adenomatosis, hepatocellular carcinoma, insulinoma, intraepithelial neoplasia, interepithelial squamous cell neoplasia, 5 invasive squamous cell carcinoma, large cell carcinoma, leiomyosarcoma, lentigo maligna melanomas, malignant melanoma, malignant mesothelial tumors, medulloblastoma, medulloepithelioma, melanoma, meningeal, mesothelial, metastatic carcinoma, mucoepidermoid carcinoma, 10 neuroblastoma, neuroepithelial adenocarcinoma nodular melanoma, oat cell carcinoma, oligodendroglial, osteosarcoma, pancreatic polypeptide, papillary serous adenocarcinoma, pineal cell, pituitary tumors, plasmacytoma, pseudosarcoma, pulmonary blastoma, renal 15 cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, serous carcinoma, small cell carcinoma, soft tissue carcinomas, somatostatin-secreting tumor, squamous carcinoma, squamous cell carcinoma, submesothelial, superficial spreading melanoma, 20 undifferentiated carcinoma, uveal melanoma, verrucous carcinoma, vipoma, well differentiated carcinoma, and Wilm's tumor.

126. The combination of Claim 115 wherein the  
25 matrix metalloproteinase inhibitor is selected from  
compounds, and their pharmaceutically acceptable salts  
thereof, of the group consisting of:

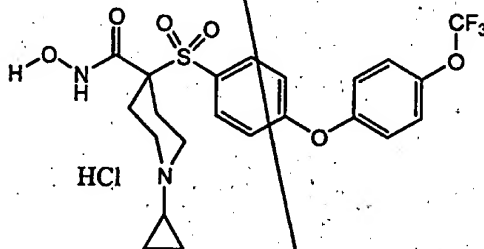
-403-

1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

2)



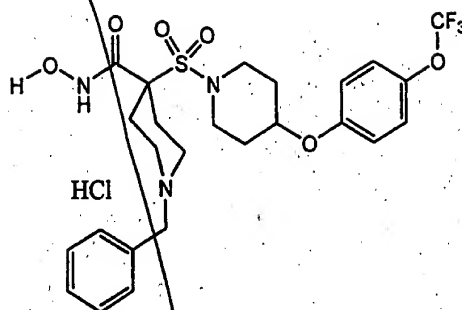
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

105005" 00039860

Sub 1  
Cont

-404-

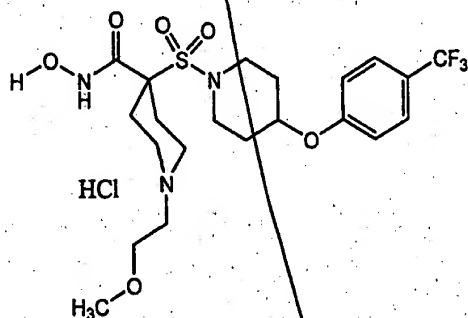
3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

5

4)



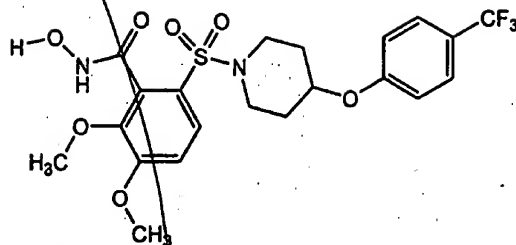
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

10

Sub: Cont

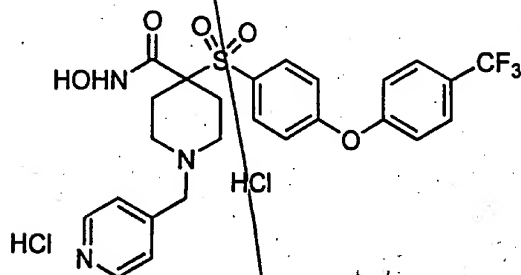
-405-

5)



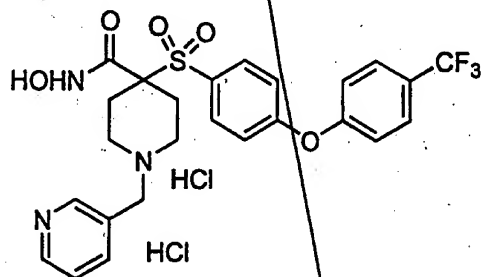
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)



N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

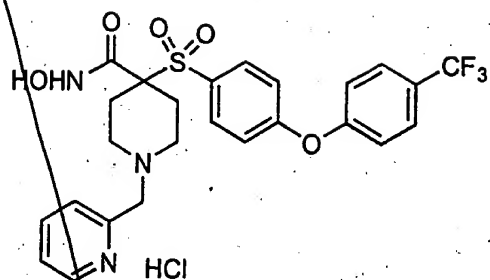
T05001-9909360

*Sub a  
cont*



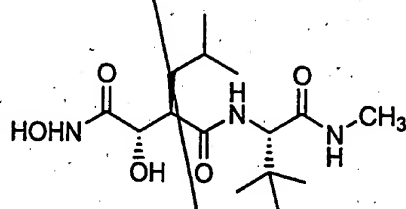
-406-

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)

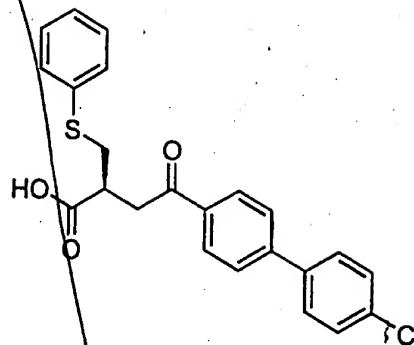


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*), 2R\*, 3S\*]]-,

Suba!  
cont

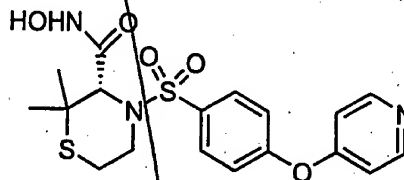
-407-

10)



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]- 4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2  
dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl] 3-  
thiomorpholinecarboxamide,

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),  
6-demethyl-6-deoxy-4-  
dedimethylaminotetracycline,

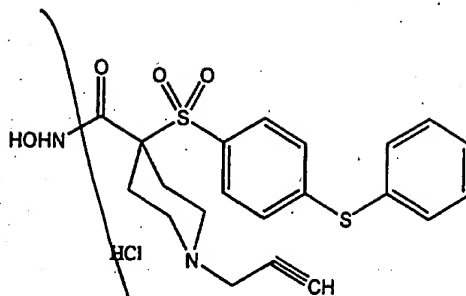
13) Chiroscience D-2163, 2- [1S- ([ (2R,S)-  
acetylmercapto- 5- phthalimido]pentanoyl- L-  
leucyl)amino- 3- methylbutyl]imidazole,

09866063-100501

*See 1  
Cont*

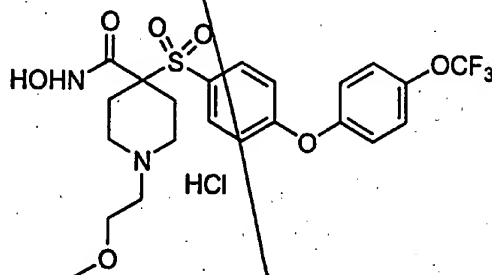
-408-

14)



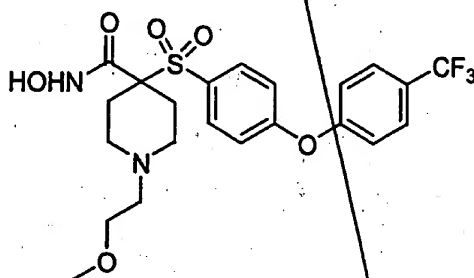
N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-  
1-(2-propynyl)-4-piperidinecarboxamide  
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethoxy) phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide monohydrochloride,

16)

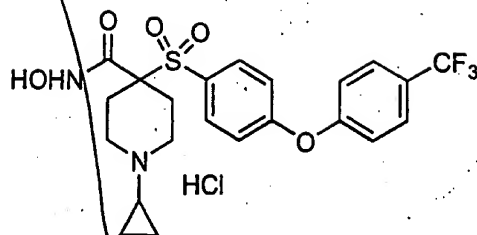


N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide,

Sub a  
Cont

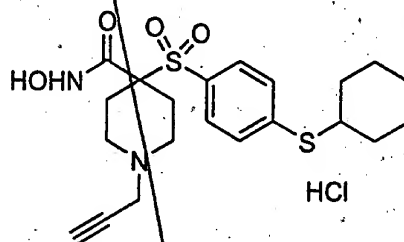
-409-

17)



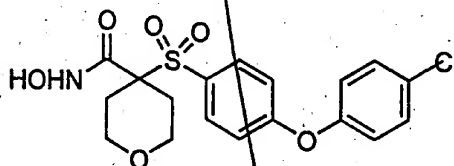
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

19)



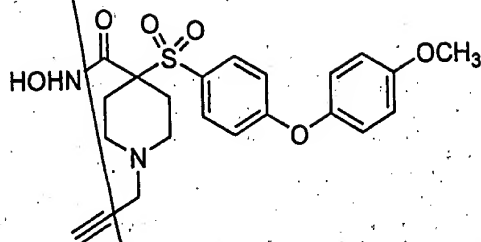
4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

09868063 10501

Sub 1  
Cont

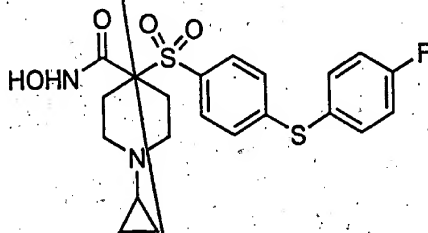
-410-

20)



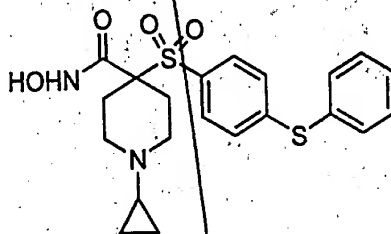
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl]sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-[(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)



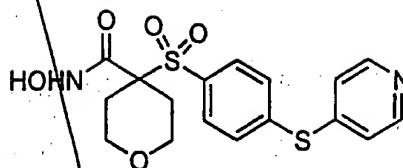
1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

0956063700501

Sub a Cont

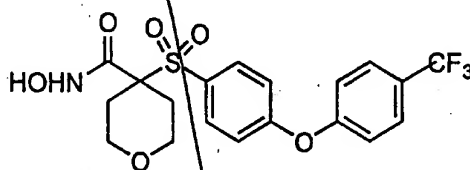
-411-

23)



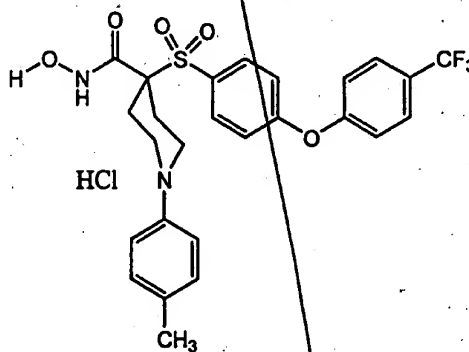
tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

24)



tetrahydro-N-hydroxy-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-2H-pyran-4-carboxamide.

127. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



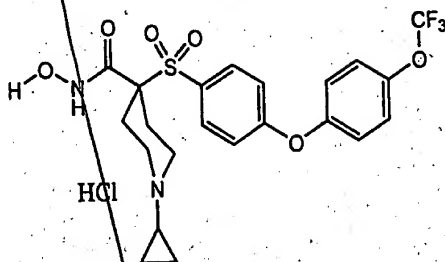
N-hydroxy-1-(4-methylphenyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

09868063 100501

*Sub a  
cont*

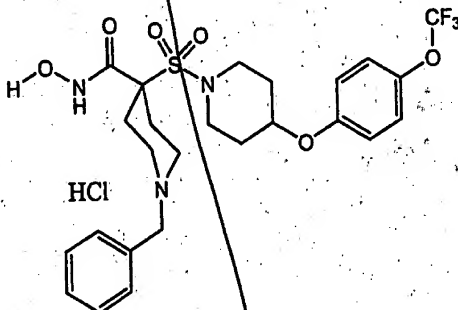
-412-

128. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



1-cyclopropyl-N-hydroxy-4-[[4-[(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

129. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



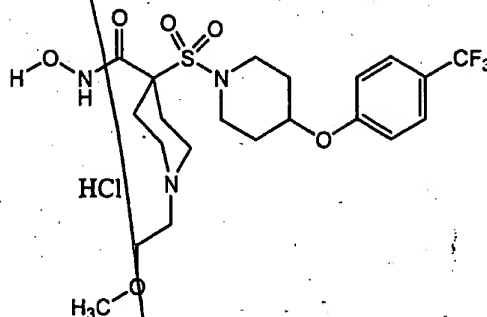
N-hydroxy-1-(phenylmethyl)-4-[[4-[(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

096606100001

Sub  
A1  
cont

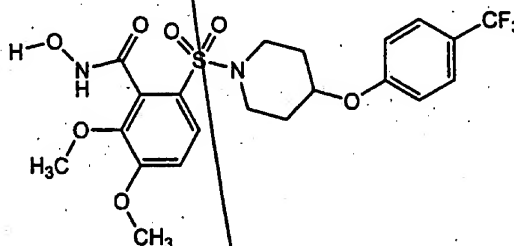
-413-

130. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

131. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



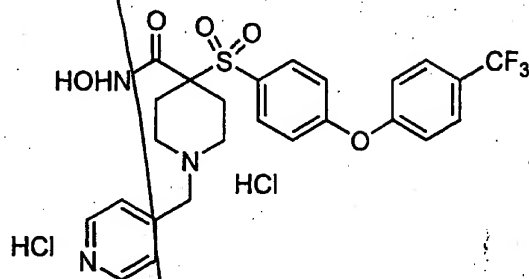
10 N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide.

098630610001

*Sub a!  
cont*

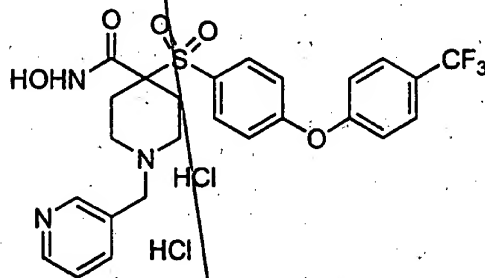


132. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

133. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



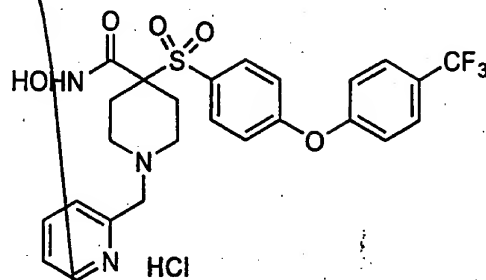
N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride.

09863067

Suba  
rent

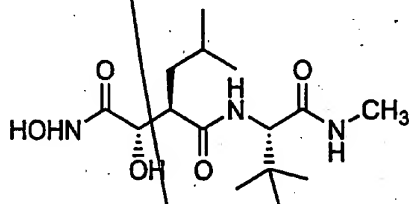
-415-

134. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride.

135. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



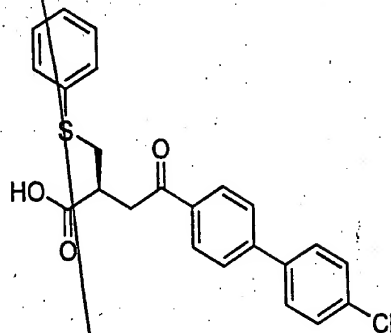
British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*), 2R\*, 3S\*]]-.

00368061001

*Suba  
cont*

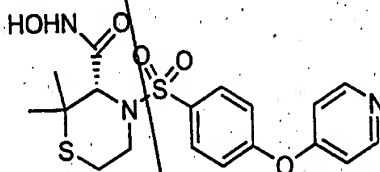
-416-

136. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



5 Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]-4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid.

137. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is



15 Agouron Pharmaceuticals AG-3340, N-hydroxy-  
2,2-dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl]-3-  
thiomorpholinecarboxamide.

138. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is CollaGenex  
Pharmaceuticals CMT-3 (Metastat), 6-demethyl-6-deoxy-4-  
20 dedimethylaminotetracycline.

139. The combination of Claim 115 wherein the matrix metalloproteinase inhibitor is Chiroscience D-

TOC00129089860

*Sub a cont*

-417-

2163, 2- [1S- ([ (2R,S)- acetylmercapto- 5-phthalimido]pentanoyl- L- leucyl)amino- 3-methylbutyl]imidazole.

5 140. The method of Claim 1 wherein the antineoplastic agent is anastrozole.

141. The method of Claim 1 wherein the antineoplastic agent is calcium carbonate.

10

142. The method of claim 1 wherein the antineoplastic agent is exemestane.

15 143. The method of Claim 58 wherein the combination is administered in a sequential manner.

144. The method of Claim 58 wherein the combination is administered in a substantially simultaneous manner.

20

145. The method of claim 1 wherein the antineoplastic agent is exemestane.

146. A method for treating or preventing a neoplasia disorder in a mammal in need of such treatment or prevention, which method comprises administering to said mammal a therapeutically-effective amount of a combination of a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor, wherein said matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

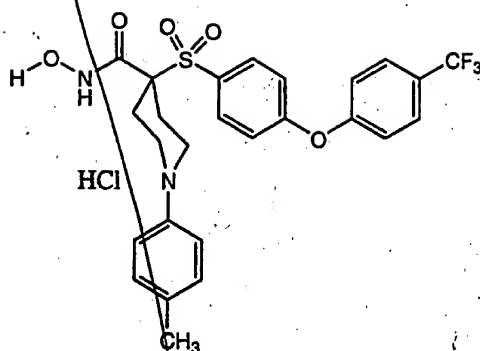
25  
30

09668063-10561

Sub 1  
Cont

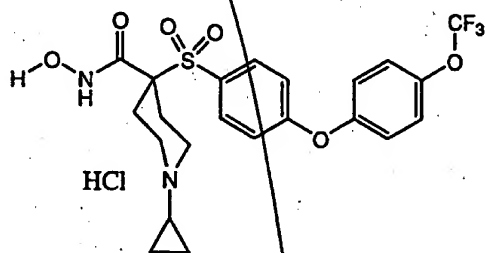
-418-

1)



N-hydroxy-1-(4-methylphenyl)-4-[[4-[(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

2)



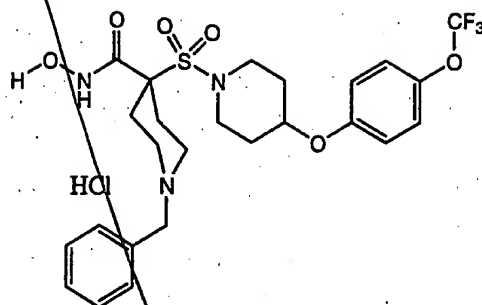
1-cyclopropyl-N-hydroxy-4-[[4-[(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

T05001 "C000000" 100501

Sub 1  
cont

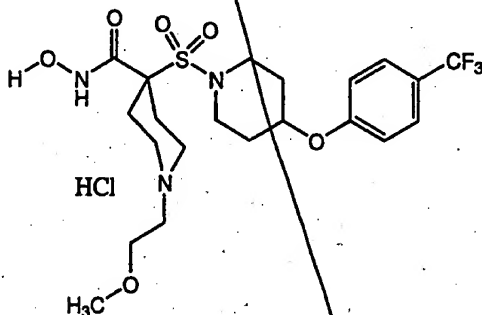
-419-

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

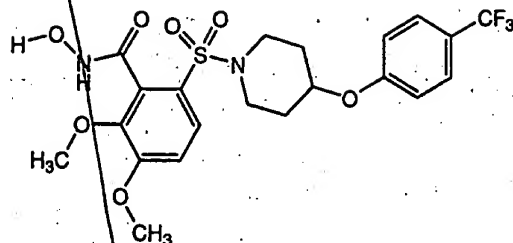
4)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

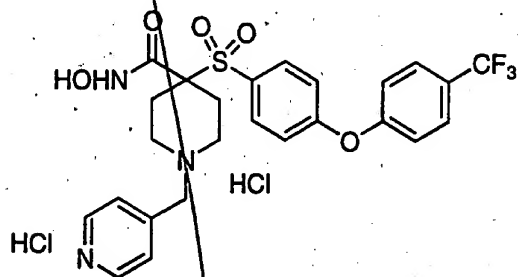
Footnote 1  
cont

5)



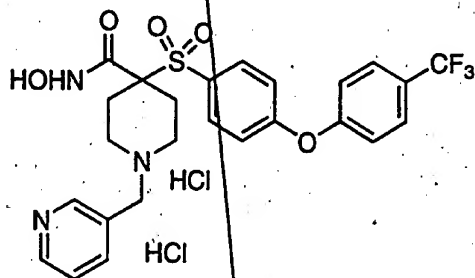
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

7)

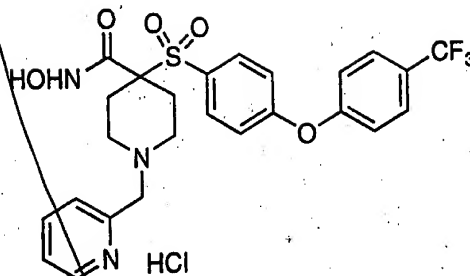


N-hydroxy-1-(3-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

*but a fort*

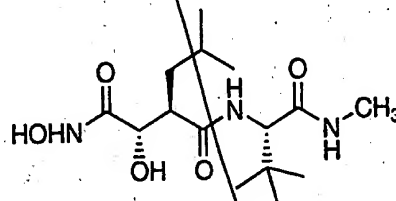
-421-

8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

9)

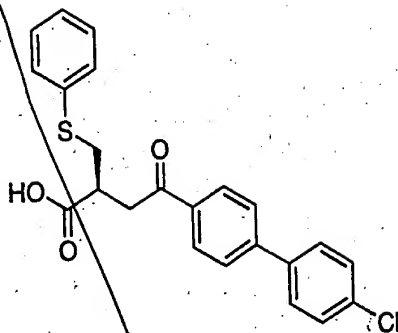


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*),2R\*,3S\*]]-,

Suba  
cont  
105001-105001

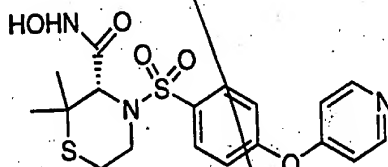


10)



Bayer Ag Bay-12-9586, 4-[(4'-chloro[1,1'-  
iphenyl]-4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid,

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2-  
dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl]-3-  
thiomorpholinecarboxamide,

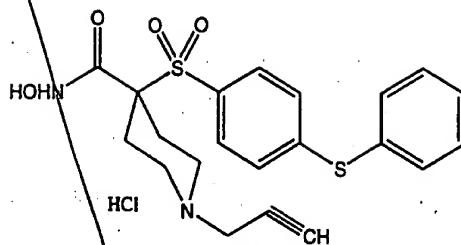
12) CollaGenex Pharmaceuticals CMT-3 (Metastat),  
6-demethyl-6-deoxy-4-  
dedimethylaminotetracycline,

13) Chiroscience D-2163, 2- [1S- ((2R,S)-  
acetylmercapto- 5- phthalimido]pentanoyl- L-  
leucyl)amino- 3- methylbutyl]imidazole,

005001-100501  
 Sub a  
 cont

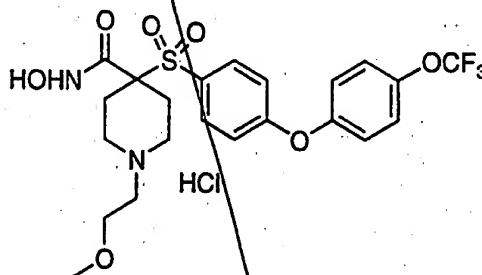
-423-

14)



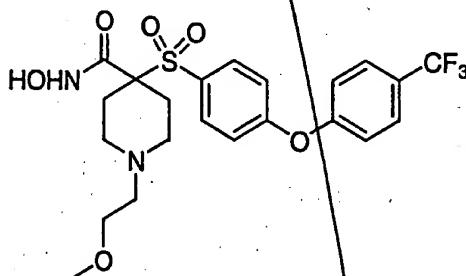
N-hydroxy-4-([4-(phenylthio)phenyl]sulfonyl)-  
1-(2-propynyl)-4-piperidinecarboxamide  
monohydrochloride,

15)



N-hydroxy-1-(2-methoxyethyl)-4-([4-(4-  
(trifluoromethoxy) phenoxy]phenyl]sulfonyl)-4-  
piperidinecarboxamide monohydrochloride,

16)



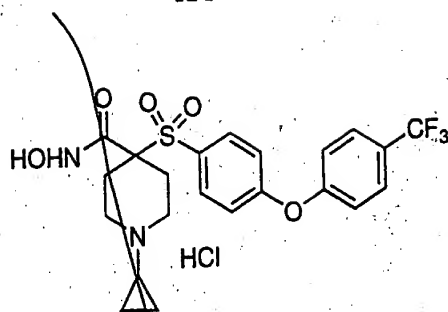
N-hydroxy-1-(2-methoxyethyl)-4-([4-(4-  
(trifluoromethyl)phenoxy]phenyl]sulfonyl)-4-  
piperidinecarboxamide,

09368063-300501

*Sub a cont*

-424-

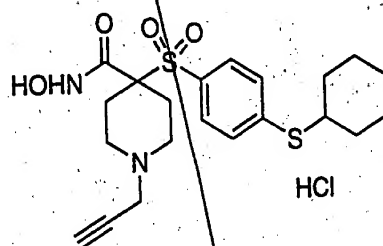
17)



1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

5

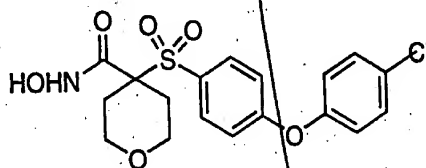
18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

10

19)



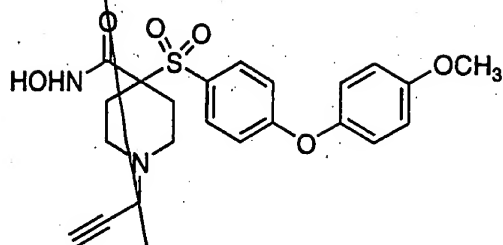
4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

15

Sub 1  
Cont  
09863063100501

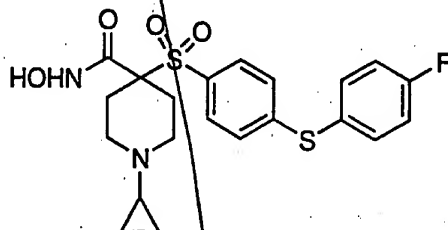
-425-

20)



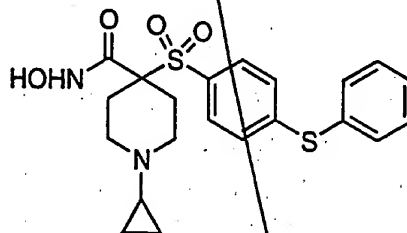
N-hydroxy-4-[[4-(4-methoxyphenoxy)phenyl)sulfonyl]-1-(2-propynyl)-4-piperidinecarboxamide,

21)



1-cyclopropyl-4-[[4-[4-(4-fluorophenyl)thio]phenyl]sulfonyl]-N-hydroxy-4-piperidinecarboxamide,

22)



1-cyclopropyl-N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-4-piperidinecarboxamide,

**SECRET**

Sub a cont

10

15

O=C(O)C1(C(=O)S(=O)(=O)c2ccc(SC3=CC=CC=C3)cc2)OCCO1

5

OC(=O)C1(C(=O)S(=O)(=O)c2ccc(Oc3ccc(C(F)(F)F)cc3)cc2)CCCCO1

10

20

25

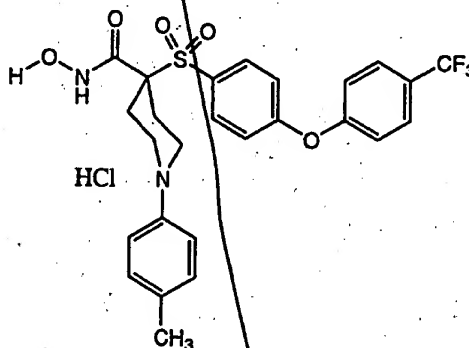
-427-

ursodeoxycholic acid, sulindac sulfone and eflornithine (DFMO).

148. The method of Claim 146 comprising  
5 administering to said mammal a therapeutically-effective amount of a combination of radiation, a cyclooxygenase-2 inhibitor and a matrix metalloproteinase inhibitor.

149. A combination comprising a cyclooxygenase-2  
10 inhibitor and a matrix metalloproteinase inhibitor, wherein said matrix metalloproteinase inhibitor is selected from compounds, and their pharmaceutically acceptable salts thereof, of the group consisting of:

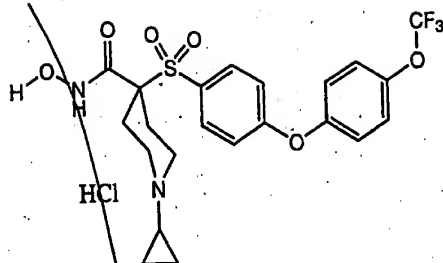
1)



15 N-hydroxy-1-(4-methylphenyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

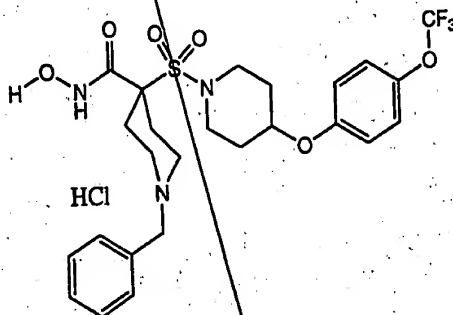
20 2)

-428-



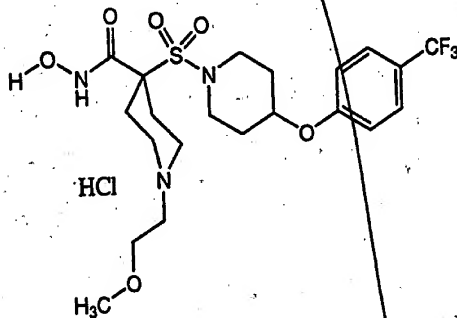
1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

3)



N-hydroxy-1-(phenylmethyl)-4-[[4-[4-(trifluoromethoxy)phenoxy]-1-piperidinyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

4)

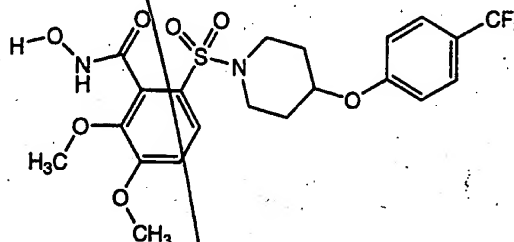


0986806100501  
Sub 1  
Cont

-429-

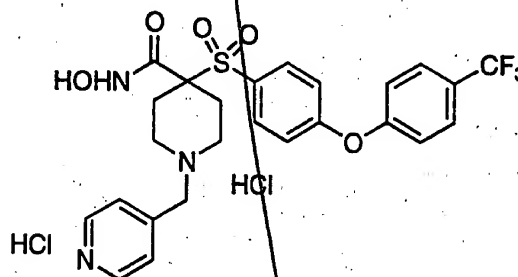
N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

5)



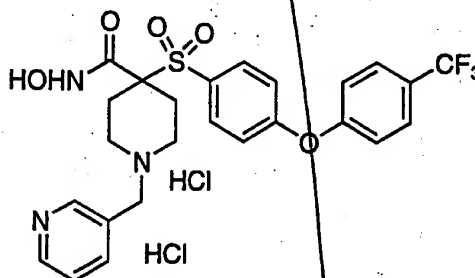
N-hydroxy-2,3-dimethoxy-6-[[4-[4-(trifluoromethyl)phenoxy]-1-piperidinyl]sulfonyl]benzamide,

6)



N-hydroxy-1-(4-pyridinylmethyl)-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide dihydrochloride,

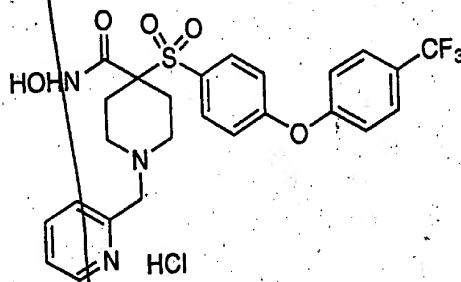
7)





5

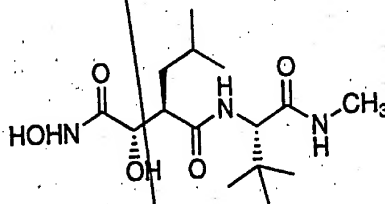
8)



N-hydroxy-1-(2-pyridinylmethyl)-4-[[4-(4-(trifluoromethyl)phenoxy)phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

10

9)

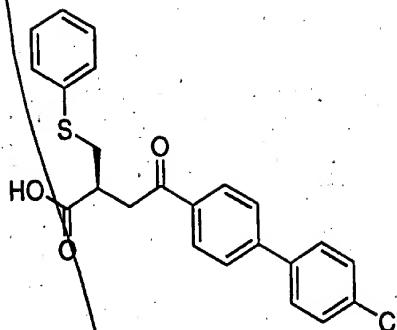


British Biotech BB-2516 (Marimastat), N4-[2,2-dimethyl-1-[(methylamino)carbonyl]propyl]-N1,2-dihydroxy-3 (2-methylpropyl)-, [2S-[N4(R\*), 2R\*, 3S\*]]-),

15

10)

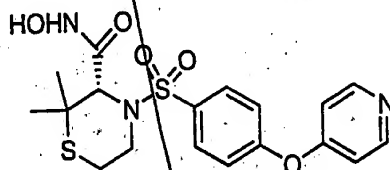
-431-



Bayer Ag Bay-12-9566, 4-[(4'-chloro[1,1'-  
iphenyl]-4-yl)oxy]-2-  
[(phenylthio)methyl]butanoic acid,

5

11)



Agouron Pharmaceuticals AG-3340, N-hydroxy-2,2  
dimethyl-4-[[4-(4-  
pyridinyloxy)phenyl]sulfonyl] 3-  
thiomorpholinecarboxamide,

10

12) CollaGenex Pharmaceuticals CMT-3 (Metastat),  
6-demethyl-6-deoxy-4-  
dedimethylaminotetracycline,

15

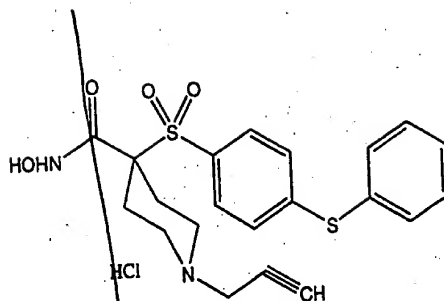
13) Chiroscience D-2163, 2- [1S- ([ (2R,S)-  
acetylmercapto- 5- phthalimido]pentanoyl- L-  
leucyl)amino- 3- methylbutyl]imidazole,

09868063100501

*Sub 1  
a  
cont*

-432-

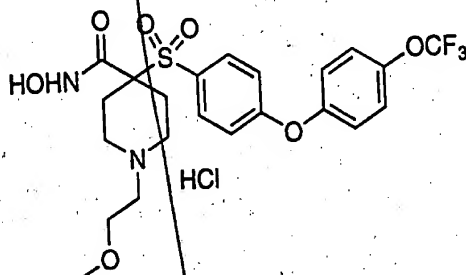
14)



N-hydroxy-4-[[4-(phenylthio)phenyl]sulfonyl]-  
1-(2-propynyl)-4-piperidinecarboxamide  
monohydrochloride,

5

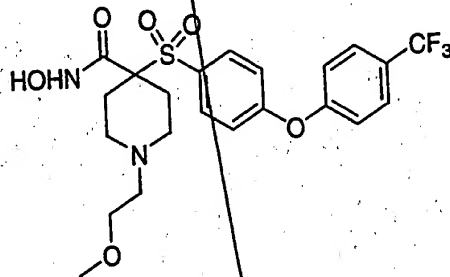
15)



N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethoxy)phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide monohydrochloride,

10

16)



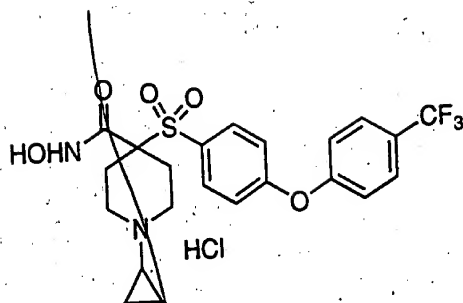
N-hydroxy-1-(2-methoxyethyl)-4-[[4-[4-  
(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-  
piperidinecarboxamide,

15

0986806-100504  
T05007908880  
Sub a  
Cont

-433-

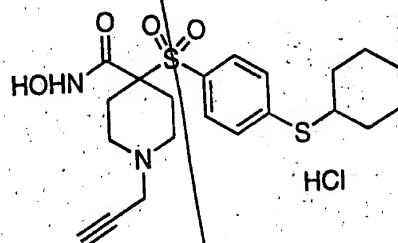
17)



1-cyclopropyl-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-4-piperidinecarboxamide monohydrochloride,

5

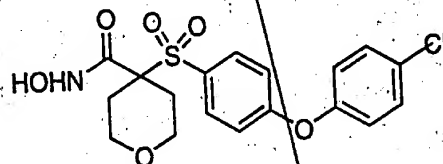
18)



4-[[4-(cyclohexylthio)phenyl]sulfonyl]-N-hydroxy-1-(2-propynyl)-4-piperidinecarboxamide monohydrochloride,

10

19)



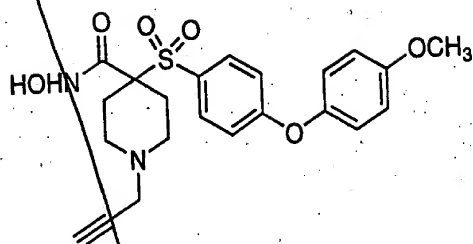
4-[[4-(4-chlorophenoxy)phenyl]sulfonyl]tetrahydro-N-hydroxy-2H-pyran-4-carboxamide,

15

Sub 1  
a  
cont

-434-

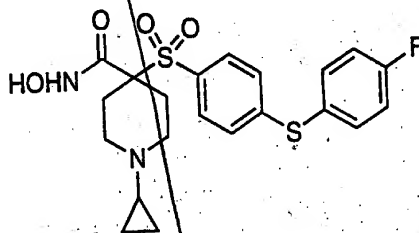
20)



N-hydroxy-4-([4-(4-methoxyphenoxy)phenyl]sulfonyl)-1-(2-propynyl)-4-piperidinecarboxamide,

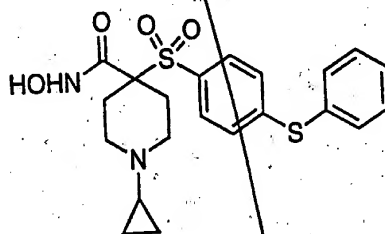
5

21)



1-cyclopropyl-4-([4-(4-fluorophenylthio)phenyl]sulfonyl)-N-hydroxy-4-piperidinecarboxamide,

22)

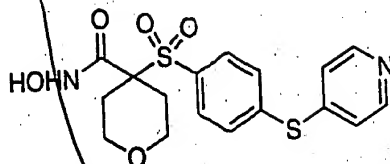


1-cyclopropyl-N-hydroxy-4-([4-(phenylthio)phenyl]sulfonyl)-4-piperidinecarboxamide,

15

TO5000-1-998860  
Sub 1  
Cont

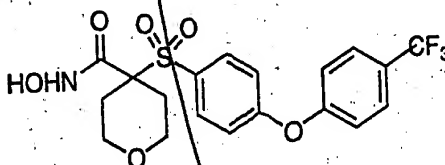
23)



tetrahydro-N-hydroxy-4-[[4-(4-pyridinylthio)phenyl]sulfonyl]-2H-pyran-4-carboxamide, and

5

24)



tetrahydro-N-hydroxy-4-[[4-[4-(trifluoromethyl)phenoxy]phenyl]sulfonyl]-2H-pyran-4-carboxamide.

10

Sub 1  
a  
Contd  
10500T-2908980  
10500T-10501